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PANEL DISCUSSION ON ADVANCES IN THE DIAGNOSIS AND TREATMENT OF CEREBROVASCULAR DISEASE*

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MODERATOR WRIGHT: This subject has been neglected for many years. Until recently, the person afflicted with a stroke was relegated to an unfortunate position on the medical, psychiatric or neurologic ward of a hospital because no one was interested in him. The attitude was that little could be done. If the patient was going to get well, he would, but he probably would not improve much. He was, in a sense, an outcast from society. People felt sorry for him, but there was no constructive program for his treatment.

In the early 1950's, various groups took a different attitude and suggested that, inasmuch as in the United States approximately 200,000 people die each year from strokes, and over 2 million of the living have had a stroke, perhaps the problem should be examined. In 1954, a conference was held at Princeton to which 40 people who had worked in this field were invited. They compiled the available information, and raised many questions that required answers.

Following this, a sudden catalytic reaction took place in many centers. The Heart Association became more interested in strokes, especially the vascular aspects. The neurologist became interested in strokes. The National Institutes of Health, both the Heart Institute and the Neurological Disease and Blindness Institute, became interested. Money became available for research.

During the intervening years much new information has been obtained. New forms of therapy have been studied, and some of them have proved helpful in certain selected cases. New forms of diagnosis and more accuracy in diagnosis have become possible. Experts now can transmit some of this information to

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those less skilled in the field, so that they too can apply it against this disease process.

Innumerable questions remain unanswered. Many more will arise in the future because of the enormous number of people who are interested and the funds that have become available.

Questions we shall discuss here are: 1) what to do for a person with a stroke—either in the developmental phase or thereafter—if the stroke has been a minor one, and 2) how to prevent subsequent strokes. In order to decide what to do, the first step is to make as accurate a diagnosis as possible. Most of you know how to make a diagnosis if the patient has hemiplegia and cannot talk, but localization of the lesion and the determination of its type are functions of one trained in the field. He need not be a neurologist, but neurologists are ahead of us in terms of special and functional diagnoses in this regard. Therefore, they should teach the internists.

I shall ask Dr. Toole to discuss the *problem of diagnosis*. Dr. Toole.

Dr. Toole: Not many years ago, a clinician could diagnose cerebrovascular disease as strokes, cerebrovascular accidents or cerebral spasms, content in the knowledge that, regardless of whether the underlying pathologic change was hemorrhage, infarction, insufficiency or embolus, the therapy consisted largely of supportive measures and was similar for all forms. Then Dr. Wright and his co-workers led the way in the use of anticoagulant medication for certain strokes, and it became imperative that accurate differential diagnosis be made so that appropriate therapy could be undertaken. Within the past few years there has been a growing realization that many cerebral episodes that have been attributed in the past to disease of the small intracranial vessels, are actually secondary to abnormalities of the carotid and vertebral arteries themselves and not of their arborizing intracranial branches. From this discovery is evolving the concept that surgical repair of diseased carotid and vertebral vessels may play a role in the management of certain cerebrovascular lesions.

Because of these two major advances—anticoagulant therapy and vascular repair—the precision of etiologic diagnosis and the exact anatomic localization of neurovascular lesions have become vital for the proper selection of therapeutic methods.

The frequency with which cerebral and brain-stem syndromes are caused by abnormalities within the carotid and vertebral vessels is not fully known, but pathologic and arteriographic studies of patients with cerebrovascular disease indicate that from 6 to 40 per cent of cerebrovascular insufficiency and infarction syndromes may involve lesions in the carotid or vertebral vessels which contribute in large measure to the clinical picture.

Because of this, I should like to emphasize certain anatomic features that are pertinent to a discussion of these vessels. As the vertebral arteries ascend in the neck, they join to form the basilar artery which supplies the major portion of the brain stem and the cerebellum. The posterior cerebral arteries, which are in effect a continuation of the basilar artery, supply the occipital lobe of the cerebral hemisphere. It is for this reason that many people suffering from basilar or vertebral-basilar syndromes have intermittent episodes of visual abnormality.

In the past it has been assumed that, because there is a cerebral abnormality in an area supplied by a vessel, the causative pathologic lesion must lie within the arteries nourishing that area of brain. For example, it has been assumed in the case of a posterior-cerebral-artery syndrome that the abnormality lies within that artery or its smaller branches. However, more and more investigators are beginning to believe that the cause is dual, *i.e.*, there is an abnormality within the intracranial vessel, but there is also a large contributing factor from the carotid and vertebral vessels in the neck.

It is important to note that the vertebral artery is the first branch of the subclavian artery. It ascends to the level of the sixth cervical vertebra in most people, and then continues through the transverse formina of the cervical vertebrae surrounded by a bony canal to the level of the atlas and the axis, where it ascends through the foramen magnum to form the basilar artery by joining with its counterpart from the opposite side. The importance of the bony canal in which the vertebral artery travels is just beginning to be recognized. It was seldom studied in the past, because dissections of this area are difficult to perform in routine anatomic work. Therefore, it was not realized that osteoarthritic changes in these cervical vertebrae could cause impingement upon the vertebral artery as it traverses these canals.

Another possibility that is being studied, but is not proved at this time, is that there may be variation in the blood flow through the vertebral arteries as the head is placed in various positions with relation to the neck. If the head is turned, there is a torsion movement of the atlas upon the axis. With this torsion or rotating movement, the anatomic relationships are changed. To take a common condition as an example, in a person with a small vertebral artery on one side and a large one on the other, certain positions of the head in relation to the neck would cause impingement on the large vertebral vessel and impede the flow. We conceive of this as occurring in people with arthritic syndromes.

The variety of syndrome with which disease of the carotid, vertebral or basilar artery becomes manifest is dependent upon many factors. The existence of a vascular lesion does not necessarily mean that a clinical syndrome will accompany it. This would depend upon the many additional factors such as the condition of the circle of Willis, congenital variations in vessel anastomoses, the effects of disease (primarily arteriosclerosis), systemic variations in cardiac output, or the presence of anemia. The circle of Willis, which joins the basilar artery and the two carotid arteries, is frequently anomalous. The variations in the circle of Willis are so striking from person to person that it is difficult to predict with assurance what collateral blood supply will be available for a patient suffering, for example, from disease of the internal carotid artery. It might be that, if the carotid artery were completely occluded, there would be enough collateral supply through the posterior communicating artery and through the anterior communicating artery so that no clinical symptomatology would be caused by the loss of this vessel. In other instances, however, mere stenosis of the internal carotid artery in a person lacking a posterior communicating artery would produce profound hemiplegia.

By far the most common cause of carotid artery thrombosis, or stenosis, is an

arteriosclerotic plaque situated in the carotid sinus just distal to the bifurcation of the common carotid in the neck. The reason for this is not known with certainty, but it is possible that as blood comes from the common carotid artery, eddy currents or forces of flow may traumatize the intima of the internal carotid sinus and produce the so-called sentinel plaque which is so commonly seen. Not infrequently, in a person who has a normal carotid vessel so far as sclerotic change is concerned, there is marked arteriosclerotic stenosis of the carotid sinus.

The anatomic relation of the ophthalmic artery to the internal carotid artery is important. It should be noted that the first branch of the internal carotid artery, above its point of origin in the neck, is the ophthalmic artery at the intracranial level. It is mentioned here in order to point out that, if at any time pressure is reduced within the internal carotid artery between its point of origin in the neck and the intracranial level, a similar reduction in pressure also occurs in the ophthalmic artery and its branch, the retinal artery. In persons with the carotid-artery syndrome, this is manifested by the monocular visual abnormalities on the ipsilateral side associated with contralateral neurologic abnormalities. For instance, a person with recurrent attacks of weakness on the right side of the body may have loss of vision in the left eye in recurrent episodes because the carotid artery on the left supplies the left eye.

A method for the measurement of blood pressure within the retinal artery is available in ophthalmodynamometry, which was discovered and used by the French as long ago as 1916. Only recently has this procedure been revived. Measurement of retinal artery pressure is of great help in the diagnosis of the syndrome of carotid-artery disease. The instrument is a spring-loaded gauge calibrated in grams. It is applied to the lateral margin of the sclera while the fundus of the eye is visualized with an ophthalmoscope. Increasing pressure on the gauge causes the retinal artery to pulsate at the optic disc. A diastolic level of pressure is achieved first, and the gauge is read. Then the instrument is reapplied to the scleral margin and the pressure is further increased. Finally, the vessel stops pulsating and becomes blanched. This is the systolic level. Pressure is measured in each eye, and the results are compared. If pressure is decreased in one retinal artery, carotid-artery disease probably exists.

In every patient suffering from cerebrovascular disease with attacks of insufficiency or thrombosis, the pressure in the retinal arteries should be measured. A short case history illustrates the reason:

> The patient was a 48-year-old butcher with slight hypertension. One day when he was using a meat cleaver, he experienced right monoparesis and aphasia for two minutes. In a few weeks, he had another such episode. When he was admitted to the hospital, a murmur was present in the carotid artery on the left side. The retinal artery pressures were measured and a significant difference was found between the systolic and diastolic levels in the two eyes, the left retinal artery pressure being lower than the right. After confirmatory arteriography the patient was subjected to endarterectomy of the left carotid artery. The pressures returned to normal—meaning that they became equal. The patient has remained asymptomatic in the two years of follow-up study, and the retinal artery pressures have remained equal.

MODERATOR WRIGHT: Thank you, Dr. Toole. I hope that we shall have time to bring out some of the questions you have not had an opportunity to cover.

One of the problems in the therapy of cerebrovascular, as well as all other disease, is *how to establish the value of a new method.* In order to accomplish this, one must use random sampling for both control and treated series.

Dr. Groch is the director and co-ordinator of a study which has been under way at Bellevue Hospital for more than three years. It is a joint effort on the part of the Medical and Neurological Services of Cornell, the Medical Services of Columbia, and the Rehabilitation Service of New York University. It is a large project, but the selection of cases has been based on a random sampling method. I shall ask Dr. Groch to tell you about the technic and the results to date.

DR. GROCH: This study did not begin *de novo*, but had its roots in the work of several investigators, among them Dr. Wright and his associates at New York Hospital, Dr. Millikan and his associates at the Mayo Clinic, and Dr. Miller Fisher and his associates at the Massachusetts General Hospital.

One aspect of the study is the evaluation of anticoagulants in the treatment of cerebrovascular disease. A plan was set up whereby equal numbers of patients, taken at random, fell into one of two categories—a treatment group or a control group. This was accomplished as follows:

When a patient enters Bellevue Hospital and is admitted to either the Cornell or Columbia Medical Service or directly to the Cornell Neurology Service, he is seen by a member of the cerebrovascular study group and a complete examination is performed. The cerebrospinal fluid is examined. An electrocardiogram is obtained, and a complete blood count is made. The stool is examined. If anticoagulant therapy is believed to be suitable, the patient is submitted to a previously randomized selector system. A card is pulled which indicates whether he is to be treated or is to serve as a control. No matter what happens to the patient thereafter, he is kept in the designated category. This point is emphasized, because some members of the house staff at Bellevue Hospital believe that anticoagulants should be used for the treatment of every stroke. If a patient falls into the randomized control group, and suddenly his clinical status becomes worse, it is sometimes difficult to persuade the house staff to let the clinical course evolve without anticoagulant therapy.

For good reason, we do not interfere with the patient's program once he has been randomized, because the course can be extremely variable. Until large numbers of patients are assembled and compared—control groups against treatment groups—we shall not be able to state what role anticoagulant therapy plays in the treatment of strokes.

This study has continued for slightly less than three years, and we have some interesting results. During this period, we have seen 445 patients with all types of cerebrovascular disease, including cerebral hemorrhage, cerebral embolism and thrombosis. Of these, 69 patients were drawn for the control group and 79 for the treatment group, the total of 148 comprising one-third of the 445 patients.

Thus, we have found that only about one-third of the patients with cerebrovascular disease entering a large general hospital such as Bellevue are suitable

for anticoagulant therapy. The other patients were excluded because: 1) we were "obliged" to treat them, or 2) they were not suitable for randomization. In the first category were those patients who had myocardial infarction in association with the stroke or who had had rheumatic heart disease and a secondary cerebral embolus; such patients should be treated with anticoagulants. One hundred and fifty-six patients (approximately 40 per cent) were not suitable for randomization. They either had bloody or xanthochromic cerebrospinal fluid, or they were so critically ill that they could not be evaluated before death.

At present (April 30, 1959) 23 patients still are being treated with anticoagulants under our long-term plan. There has been a definite decrease in the number of patients who can be followed after the institution of anticoagulants. Among patients for whom anticoagulant therapy could not be continued after they had been randomized, the reasons were: 4 had hemorrhagic complications while in the hospital, 6 died in the hospital, 3 were unable to attend our long-term anticoagulant clinic, and 9 were transferred to other institutions. One patient had a social problem which would have prevented regular attendance at the clinic. Some of these problems occur in private practice whereas others do not, but they will arise in any group of patients in a large municipal hospital and in a fair number of patients in private practice. Various complications may prevent the continuance of anticoagulant therapy once the patient leaves the protective environment of the hospital. Chief among such causes in our group was inability to attend the outpatient clinic. This applied especially to hemiplegic patients, who could not get about as well as, for example, patients with myocardial disease. Control of anticoagulant therapy was poor in only 3 patients. Once the patient's requirement was stabilized, anticoagulant regulation was not difficult. Hemorrhagic complications occurred in some of the out-patients. These were not severe except in one case. There have been no deaths due to anticoagulant therapy.

The incidence of *hemorrhagic complications* increased decade by decade. Perhaps this should be expected, because the number of complicating diseases which may cause bleeding in patients who are receiving anticoagulants obviously will increase with age. Nevertheless, age *per se* is not a contraindication to anticoagulant therapy. We have treated patients in their 70's without difficulty. However, in dealing with an elderly patient, one must be cautious and make certain that he knows what you mean when you ask him whether or not he has had any bleeding. Sometimes it is imperative to deal with the patient's relatives. Hemorrhagic complications occurred in 20 per cent of patients in our treatment series, and in 1 control patient. The control patient was interesting. This man was admitted to the Columbia Medical Service and was subjected to the randomization procedure after it was decided that he had a cerebral thrombosis. He was selected as a control, and recovered fairly well from his stroke. Three weeks after discharge from the hospital, he was readmitted to the hospital with a gross cerebral hemorrhage. Had we given this patient anticoagulant therapy, we probably would not have been able to continue our study on the Columbia Service. This event demonstrates the vagaries of clinical therapy that have to be taken into account when the final summation of the results in these patients is prepared.

In 16 patients there have been major hemorrhagic complications, and in 2 there have been minor complications such as epistaxis.

Thrombo-embolic complications have occurred, subsequent to randomization, in 20 per cent of patients not treated with anticoagulants, and in 8 per cent of the patients who were treated. Among the latter group, 1 patient had a prothrombin time in the therapeutic range, and 4 patients had not been receiving anticoagulant therapy for as long as sixty-five days at the time another thrombo-embolic complication occurred. Thus, although the incidence of thrombo-embolic complications was 8 per cent, only 1 patient was receiving wholly adequate therapy at the time of complication.

There were 16 deaths among patients who did not receive anticoagulants, and 11 deaths among patients who received anticoagulants. It is noteworthy that the numbers of deaths not due to thrombo-embolism were equal in both groups, yet the numbers of deaths due to thrombo-embolism were greater in the group that has not received anticoagulant therapy.

This is a small study to date, but these findings have been consistent year by year as we have randomized our patients and analyzed our figures. There appears to be a trend. If our results continue along these lines, we may be able to say that anticoagulant therapy plays a protective role in patients with cerebral thrombosis.

It seemed pertinent to review the records of our patients who had been in the out-patient clinic for more than a year, and who had been maintained continuously with anticoagulant therapy. We wished to see how often the prothrombin time fell below or above the therapeutic range, *i.e.*, between 25 and 40 seconds. Only a few prothrombin times were below the therapeutic range.

Fortunately, to date, we have had no deaths due to hemorrhage in any of the patients in the randomized series.

MODERATOR WRIGHT: Thank you, Dr. Groch.

This is a serious and critical effort to find the answer to a vital question. As Dr. Groch indicated, it is in part an outgrowth of a study we had been carrying on for approximately ten years, in which we used patients as their own controls. They were not randomized, but served as their own controls during periods when anticoagulant therapy was discontinued for various reasons. At least, each patient was the same biologic entity, except as all human beings vary from year to year.

In that study, during a period of 2500 months, among 90 persons who had had their first stroke, 212 additional thrombo-embolic episodes occurred, of which 62 were cerebral. The same patients, while receiving anticoagulant therapy for a total of 2200 months, had only 68 additional thrombo-embolic episodes, of which 15 were cerebral. This is a different way of studying the project on a long-term basis. Dr. Groch's investigation covers a shorter period of observation and his cases are handled in a different way, but the end-results have been equally encouraging.

Next, we shall consider *the contribution of surgery to treatment.* The repre-

sentative of an active group from Baylor University, Dr. Crawford, will tell us what he thinks about the status of surgery today.

Dr. Crawford: Thus far, the surgical therapy of strokes has been applicable only to those obstructive vascular lesions located outside the head. These lesions are a cause of stroke in 40 per cent of patients referred to us with this disease. They assume certain characteristic locations: 1) the internal carotid arteries as they originate from the common carotids, 2) the vertebral arteries as they originate from the subclavian arteries, and 3) the great vessels at or near their origin from the aorta. In most instances the disease remains localized to these areas for some time after the onset of symptoms, but as the pathologic changes of atherosclerosis progress to complete occlusion, a thrombus forms distally and this may progress rapidly up the involved vessel into the head.

What is the natural course of this disease? It is difficult to say. In a review of the literature, I found reports on 150 patients proved by arteriography to have these lesions located outside of the head and who were followed from one to five years. Only 25 per cent experienced a spontaneous recovery in this period of time, owing to the presence and further development of collateral circulation. Thirty-three per cent had a residual neurologic deficit not severe enough to prevent them from carrying on to some degree. Thirty-three per cent required some type of institutional care. Approximately 10 per cent died.

For the following reasons, among others, operation is indicated: 1) these extracranial lesions are usually localized and occur in an artery that is large enough to permit a definitive surgical procedure; 2) regardless of the treatment employed (short of removing the obstruction), recovery can otherwise take place only through the development of collateral circulation and this is often hampered by the high incidence (more than 50 per cent) of multiple lesions with partial or complete occlusions in the remaining vessels of the head; and 3) the operation is a direct attack on the pathologic condition and comes close to restoring normal circulation. Moreover, 35 per cent of our patients are referred to us because they either were not improved or grew worse despite receiving anticoagulant therapy. It is of interest that 5 patients experienced strokes while receiving anticoagulant therapy for heart disease.

All patients with strokes, in whom the neurologist can exclude brain tumor or brain hemorrhage, should be studied by arteriography. When insufficiency of the internal carotid artery is suspected, bilateral carotid arteriograms can be obtained under local anesthesia.

Occlusion may be either partial or complete. A good candidate for operation is one with partial occlusion of the internal carotid artery at its origin. These lesions always are operable and with the present state of surgical knowledge, circulation invariably can be restored. Complete obstruction of the internal carotid artery is almost invariably due to short atheromata with a superimposed thrombus. If there is an opportunity to operate upon a patient before the thrombus becomes organized, it can be pulled out like an angleworm out of a hole. By doing that and removing the atheroma, circulation can be restored.

The operation varies with the location of the lesion. It is performed under

local anesthesia. In the vertebral and the carotid arteries, there is no problem about removing the obstruction. The technical problem is closure of the arteriotomy wound in such a way as to avoid stricture and recurrent obstruction. We have tried various technics. In one, we mobilize the common and the internal carotid, transect the common carotid just below the bifurcation, and perform an endarterectomy in the diseased area, based on peeling back the normal outer layers from the atheromatous mass. Beyond the area of disease, the intima with the contained mass breaks off smoothly; then circulation is restored by end-to-end anastomosis.

The suture line has to be placed in the large artery, which can stand narrowing without producing recurrent obstruction. In another approach, a longitudinal arterectomy is performed through the atheroma, which is removed by developing a plane of cleavage between the intima and media. To prevent narrowing of the artery as a result of direct suture of the arteriotomy wound, closure is usually accomplished by sewing in an elliptical patch cut from an arterial prosthesis of knitted Dacron. In some situations, when endarterectomy would be difficult, a bypass graft is indicated.

In a few patients, distal circulation must be provided during the operation. In cases involving the great vessels or the vertebral arteries, and in most cases of internal carotid artery obstruction, it usually is not necessary. However, when there is complete obstruction of the opposite carotid, or when the patient cannot tolerate a test period of occlusion, some type of internal or external shunt must be provided to maintain blood flow past the area of operation. If symptoms develop immediately upon compression, a shunt consisting usually of a 10-cm. length of plastic tubing (4–5 mm. outside diameter) is inserted into the proximal and distal relatively normal areas of the artery through a longitudinal incision made in the diseased area. Tapes, previously placed about the proximal and distal unopened vessels, are tightened to prevent leakage of blood around the outside of the shunt. The diseased intima is then removed by working around the tube. At the completion of the procedure, as the last few sutures are being placed to close the arteriotomy, the shunt is removed.

In our series of patients with vertebral artery insufficiency or symptoms of so-called basilar artery thrombosis, 65 per cent have had lesions in the neck outside of the head. To demonstrate these abnormalities the subclavian and the vertebral artery must be visualized, as most of the lesions are at the junction of the two vessels. Arteriography is performed under local anesthesia. Surgical attack on the disease in these vessels is usually directed at the vertebral-subclavian juncture. In one type of operation, we open the larger subclavian artery opposite the origin of the vertebral artery and perform an endarterectomy, working on the mouth of the vertebral artery through the larger subclavian vessel. Usually, however, a transverse incision in the subclavian is carried longitudinally through the first portion of the vertebral artery, the plaque removed, and the vessels closed (again using an elliptical Dacron patch to prevent narrowing).

In some patients the lesion is located at the origin of the great vessels where they arise from the aorta. The operation of preference, because of its simplicity

and the accuracy with which circulation can be restored beyond the disease, is a bypass graft that extends proximally from the unobstructed aorta to the distal segments beyond the obstruction.

In 106 patients we have operated upon 149 lesions, which lends emphasis to their multiple nature. Circulation was restored in the majority of those that were operable, that is, localized. The degree of restoration varied somewhat with the type of lesion and its location. In the great vessels having disease localized to their aortic origins, circulation was restored in every case. In distal lesions of the internal carotid and vertebral arteries that were incompletely obstructing, circulation was restored in the majority of cases. In complete occlusions of these smaller vessels, circulation was restored in only an occasional case operated on soon after the onset of symptoms.

The results in this entire group of patients to date have been as follows: Approximately 40 per cent had recurring episodes, but at the time of operation had no neurologic deficit; these patients (with 3 exceptions) have had no recurrent problems since operation. The remaining 60 per cent had a neurologic deficit of some type, including complete hemiplegia in 6 instances; these patients were either significantly or completely improved except for 3 with complete hemiplegia that had been in existence for five or more days. There were 4 deaths in the entire series.

The first operation was performed a little over five years ago, but the majority were performed in the past eighteen months. Admittedly, this is not a long follow-up period. Three patients had recurrent difficulty after operation. One suffered a stroke on the opposite side due to progressive obstruction in the contralateral carotid artery; we did not suspect this lesion, because at that time we were not studying all the arteries as we do now. In the second patient, after we devised a method of outlining the vertebral arteries we found that vertebral-artery obstruction was the cause of continuation of symptoms. The third patient had a recurrence because of a poor operation.

MODERATOR WRIGHT: This interesting and provocative approach opens a broad field for further investigation.

Attention should be called to several points. Dr. Crawford presented his statistics in terms of patients referred to the clinic, and said that about 40 per cent were suitable for this procedure. I submit that this is a selected group and is not representative of the total group of patients with strokes. It is selected in the sense that these are patients whom other physicians assume have a reasonable chance of being accepted for surgery. In our own experience, taking strokes as a whole, the proportion that might be available for surgery would probably be closer to 5 or 10 per cent. This includes patients who have hemorrhagic conditions and those who have multiple thrombosis or arteriosclerotic occlusions inside the skull as well as outside. However, for patients who have an external lesion, it is a remarkable demonstration of what can be accomplished.

DR. CRAWFORD: I should like to make a comment on the matter of selection. Yes, there was a great deal of selection in the sense that we depended upon referring physicians for our cases. However, without special studies, all that one

can deduce is the section of the brain involved, except in the group of patients with lesions of the great vessels arising on the aortic arch. In this group there is diminution or absence of the pulses in the arm and neck, or a difference in blood pressure between the right and left sides. As for distal lesions, arteriography is usually the only way to discover them, although ophthalmodynamometry is of help in some instances.

MODERATOR WRIGHT: You referred to a number of cases in which arteriography and other studies had been conducted. Dr. Groch, in your series *what percentage of the total number of cases with stroke could be considered for surgery?*

DR. GROCH: We performed arteriography routinely in 69 consecutive patients in whom we thought the diagnosis unequivocally was cerebral thrombosis of the carotid-middle-cerebral tree. We found carotid occlusion in 16 per cent. These were not necessarily patients with symptoms of insufficiency; they had been admitted to the hospital as cases of stroke and then angiography had been performed.

DR. CRAWFORD: Were both bilateral carotid arteriograms and bilateral transsubclavian vertebral arteriograms obtained?

DR. GROCH: We did not perform vertebral arteriograms routinely.

DR. CRAWFORD: You would not be able to obtain accurate information without complete arteriography.

DR. GROCH: If we find an occlusion of the middle cerebral artery in a patient who has hemiplegia on the other side, we are confident that this demonstrated lesion is the cause of the hemiplegia.

MODERATOR WRIGHT: When the arterial tree is visualized up to the middle cerebral artery and a block is found in that location, and there is hemiplegia on the opposite side of the body, it seems clear where the important lesion lies.

Dr. Toole, what percentage of patients with stroke do you believe to be suitable for surgery?

DR. TOOLE: I have not investigated this problem by arteriography, but I agree with Dr. Crawford that, without definitive evidence, it is a matter of opinion. I agree, too, that several arteries must be visualized. I would make a plea for ophthalmodynamometry, because it is a screening procedure devoid of hazard. This simple bedside technic yields reliable information when the results are positive.

MODERATOR WRIGHT: Dr. Toole, to pursue this matter further, have you had experience with arteriography?

DR. TOOLE: Yes.

MODERATOR WRIGHT: What has been your experience as to the *complications of arteriography?*

DR. TOOLE: The incidence of complications varies indirectly with the skill of the physician. Every July, on our service, a new man commences to perform arteriography. The incidence of complications rises dramatically as he is being indoctrinated. It may range from 2 to 5 per cent, but as the year goes on, the procedure becomes less and less hazardous.

There is some divergence of opinion in our hospital as to whether or not ar-

teriography can be performed safely under local anesthesia, the thought being that there are more complications when it is performed under local than under general anesthesia.

MODERATOR WRIGHT: Dr. Crawford, what incidence of complications do you observe following arteriography?

DR. CRAWFORD: We prefer to perform cerebral arteriograms under local anesthesia, and usually examine at least three of the four main vessels of the head as a matter of routine. There have been 4 cases of complications from carotid arteriography. Three patients had transient convulsions with no residual abnormality. The fourth patient had received anticoagulants. He was a physician who had his own clinic. He stated when he came in that his prothrombin time had been checked and was normal; it proved to be less than 10 per cent. He had a hemorrhage in the neck requiring an emergency operation, which was successful.

Trans-subclavian vertebral arteriograms have been associated with pneumothorax in 10 per cent of our cases. Fortunately, these have not been difficult to manage, although aspiration has often been required to remove air and to re-expand the lung. Bilateral pneumothorax could be an extremely serious situation. In 1 instance, there were blebs in the apices of both lungs, which had been punctured. The patient had continuous leakage, with collapse of both lungs. Aspiration was life-saving and had to be continued by tube for five days. Recovery was uneventful thereafter.

MODERATOR WRIGHT: Dr. Groch, have you any comments about complications?

DR. GROCH: I agree with Dr. Toole that, if more than one person is performing arteriography, or if someone must be trained every year, the complication rate is high in the first month of training and then gradually decreases. It should be pointed out—Dr. Crawford, please correct me, if I am wrong—that, at Dr. Crawford's University hospitals, one or two persons perform all of the arteriograms.

DR. CRAWFORD: Several persons perform them, but each is experienced and we are able to borrow from experience obtained in the performance of arteriography in other parts of the body in about 1,500 patients with occlusive arterial disease.

MODERATOR WRIGHT: At present, arteriography is not a technic that one can acquire overnight and expect to obtain good results free from complications. It requires training and experience.

Dr. Crawford, I have a question: "*How long an interval can elapse between the onset of hemiplegia due to thrombosis of the internal carotid artery, and surgery without jeopardizing the result?*"

DR. CRAWFORD: Does that mean reversal of complete hemiplegia?

MODERATOR WRIGHT: That is what is meant.

DR. CRAWFORD: The longest interval has been twenty-three hours. One might ask why this did not occur spontaneously without operation? The particular patient was deteriorating during the 23-hour period and manifested advanced

neurologic changes. He was cyanotic and was aspirating secretions from his throat. At the time of the operation, it looked as if he would die. Dramatic changes occurred before the incision could be closed. The beginning of the reversal of the process was so quick and so dramatic that it seemed reasonable to assume that the operation could be credited with some of the improvement. Function in the hand was not restored for two weeks.

MODERATOR WRIGHT: Dr. Groch, have you a comment?

DR. GROCH: The variability in the course of lesions in the carotid artery system should be stressed. Recently we reviewed the records of 57 patients with carotid arterial disease, proved either by arteriography or by surgical exploration. We found 20 patients who had been followed without therapy for a minimum of two to three years; others had been followed for eighteen years. Several patients had had symptoms of cerebrovascular disease for nine years before they came into the hospital, and a diagnosis of thrombosis of the carotid-artery system had been established. They then lived for four to five years after discharge from the hospital without "active" therapy. The course, in some instances, has extended as long as thirteen or eighteen years.

Certain patients who have had repeated attacks may come into the hospital for an arteriogram or surgical exploration, and have a diagnosis of carotid-artery disease established. Then either without specific therapy, or following cervical ganglionectomy (performed at one time for this type of occlusion) or anticoagulant therapy, their transient ischemic attacks cease. These spontaneous remissions do occur and have also been described by Dr. C. Miller Fisher.

Therefore, there is need for a controlled study, no matter what therapeutic measure is used, before concluding that one is accomplishing "this or that" for a large group of patients. Otherwise, the conclusions are open to criticism because of the vagaries of carotid artery disease, which can manifest itself in many different signs and symptoms. Without a controlled study, one cannot state with certainty that something is being accomplished for this large group of patients. The situation is not as clear-cut as that involved in the sulfonamide therapy of meningococcal meningitis.

DR. CRAWFORD: Another interesting study is to question all patients with complete hemiplegia who come to your hospital, or are in a nursing home or old folks' home where you may be a consultant. Also interrogate their families. You will be surprised at the number of patients who had one or more small strokes before the major one. This indicates that a certain number of patients do experience complete spontaneous recovery. However, since all of the prophets are dead—Moses was the last one—it is extremely difficult to withold from a patient a simple operation which will provide him with the protection of normal circulation, especially since we have had enough experience to make it reasonably safe.

MODERATOR WRIGHT: It seems to me that we are not requesting too much when we ask surgeons to run controlled series in the same way that internists do, and to conduct randomized sampling on a large group of patients. Anticoagulants are beneficial, but this is not a satisfactorily definitive answer. We

need controlled randomized sampling of a large number of patients—not impressions about patients who are admitted from some other place or who were seen five years ago in your hospital.

Perhaps some patients may suffer because of such a program; on the other hand, the therapy may not be as good as you think it is. This has happened many times in internal medicine, and the time has come when surgeons should be willing to provide the same kind of studies conducted under critical conditions, with detailed neurologic and psychologic findings before surgery and at intervals thereafter.

When that is done, we shall have conclusive data. Until that time, no matter how fine the technic, the surgeon is in the same position as any physician who is enthusiastic about a form of therapy that he thinks works. Some patients are going to get well, and many of them will have only a minimal neurologic deficit. I incline toward the belief that surgery in these instances is a good idea; but if it is to be established conclusively, there ought to be randomized sampling. I admit that this is difficult. What do you think about it?

Dr. Toole: For the last three years, I have participated in the selection of every patient who has been admitted for carotid surgery at our hospital, and have followed each patient after surgery. We have had 13 operative cases. One patient died within thirty-six hours after surgery, because of a cerebral hemorrhage which must have been secondary to an embolism dislodged at the time of operation. All of these operations were performed by competent men under the best of conditions, and with careful and skillful technicians. It was demonstrated beyond doubt that blood flow can be re-established in a large percentage of cases.

However, there was no improvement in any of the patients who had full-blown cerebral infarction for periods longer than three hours. In 2 cases, thrombosis of the carotid artery with a cerebral syndrome developed while the patient was in the hospital; operation was performed within three hours after onset. One of the patients had a remarkable recovery; the other experienced some improvement. We have abandoned operating on patients with complete cerebral infarction, but will operate on patients who have attacks of cerebral insufficiency or recurrent episodes of ischemia, in the hope that improvement of the blood supply may prevent complete infarction.

No one can make predictions with certainty. The surgeon may believe that he is preventing future cerebral infarctions by re-establishing blood supply in persons who already have had one infarction. We can only speculate on this matter. However, I have never seen (except in the three-hour period following onset) any improvement in cerebral infarction as a result of operative intervention. In cases of cerebral insufficiency, on the other hand, surgery represents an advance in therapy.

Dr. Crawford: There is no doubt about it. The results are questionable in patients who reach a state associated with advanced neurologic change, but the unfortunate aspect of refraining from surgery in such cases is the fact that clinically one cannot make an anatomic diagnosis of the status of the brain. An ische-

mic brain and a dead brain are clinically the same—neither of them works. Occasionally, patients with severe acute arterial insufficiency resulting from central channel occlusion in the absence of collateral circulation may lapse into a nonfunctional state, but upon restoration of the circulation, dramatic functional improvement occurs.

MODERATOR WRIGHT: It is noteworthy that many persons with massive strokes, even some who lie unconscious for days with one-sided flaccid hemiplegia, make remarkable recoveries and may even go to work. Two such patients are leaving the New York Hospital now. We have given some of these patients anticoagulants, and would like to think that such treatment has helped them. However, we are unable to make a categorical statement, because patients who have not received anticoagulants have also made remarkable recoveries. The family is usually told that, even though their relative is unable to speak at this time and has complete hemiplegia, a month from today he *may* be able to speak, move and get about to a remarkable degree. These cases are baffling, but they illustrate how difficult it is to evaluate therapeutic measures. It is as difficult for internists as it is for surgeons, but we are trying to be critical about our procedure.

QUESTION FROM THE FLOOR: May I ask Dr. Crawford *what is the longest time after the onset of a stroke that one can successfully perform an operation?*

DR. CRAWFORD: We had one patient, the administrator of a hospital, who had a stroke from which she did not completely recover. The manifestations of incomplete recovery were partial paralysis on one side of the body with some aphasia. The lesion was almost complete occlusion of the internal carotid artery bilaterally. Following removal of both of these obstructions twelve months after the onset of symptoms, the aphasia cleared.

MODERATOR WRIGHT: Another question from the floor reads, "*What anticoagulant should one use?*" In general, the choice should be the one in the coumarin or phenindione group with which one is most familiar. Heparin has been used but our tendency now is not to give it immediately after a stroke. On the other hand, it seems to be indicated for the initiation of therapy when there are signs of intermittent cerebrovascular insufficiency. If others think differently, I should like to have them express their opinions.

DR. CRAWFORD: Surgery, not anticoagulants, is indicated for lesions in the neck, when it has been demonstrated that they are operable.

MODERATOR WRIGHT: One other question is, "*Are cerebral vasodilators of any value in the management of patients with cerebrovascular disease?*" Who would like to express an opinion?

DR. GROCH: The only references I can quote are the controlled studies carried out at the Mayo Clinic, and in Great Britain by Carter, with stellate-ganglion blocks and inhalations of carbon dioxide. Both groups of neurologic investigators regarded the results as nil.

PHYSICAL PROBLEMS OF PSYCHIATRICALLY HOSPITALIZED ELDERLY PERSONS*†

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A previous study in this series concerned the physical problems of 260 community volunteers past the age of 60—a group which included persons from upper and lower socio-economic levels and both white and Negro races. Limitations on physical functional capacity were found to be related inversely to socio-economic conditions and directly to increasing age. There were no differences between the patterns of illness in the various elderly age groups or in the two socio-economic groups (1).

During the collection of data from the community group and from a group of 78 elderly persons hospitalized for psychiatric illness, a strong clinical impression was gained that persons hospitalized for psychiatric illness exhibit more physical illness than do community subjects. This report is concerned primarily with a description of the physical problems of psychiatrically hospitalized persons past the age of 60 and a comparison of their problems with those of community subjects.

SUBJECTS

Seventy-eight white subjects in either John Umstead Hospital or Duke Hospital for psychiatric reasons, were examined. Their ages ranged from 60 to 89 years, and there were equal numbers of men and women.

Many persons of this age admitted to psychiatric hospitals are severely disabled owing to various forms of chronic brain syndrome. In this study, only those subjects were included who were able to communicate freely with the examiner. They were also required to participate in sociologic and psychologic testing. Thus the group was definitely more intact with regard to social functioning than are most psychiatric patients admitted to the hospital. Each patient underwent a thorough physical and neurologic examination. Psychiatric, medical, and social histories were obtained, and psychologic and laboratory tests were performed, including an electrocardiogram and electroencephalogram.

Because special efforts had been made to examine equal numbers of very old people in the community groups the psychiatrically hospitalized patients were slightly younger in mean age. They were most closely comparable to the lower socio-economic community group. In order to make comparisons valid, the two groups were matched on the basis of age, sex, race, education and occupation. This reduced the hospital group to 65, with an equal number in the matched

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community group. Exact matching was possible for age, sex, race and education. However, the community subjects had backgrounds that were more related to technical and clerical jobs and less to farm and service work, compared to the hospital subjects; this was unavoidable.

All subjects were rated as to psychiatric symptomatic category (2). As shown in Figure 1, the hospitalized psychiatric patients were classified as 67 per cent with psychotic symptoms, 29 per cent with neurotic symptoms, and 3 per cent without symptoms. Only 7 per cent of the matched community subjects had psychotic symptoms, 50 per cent had neurotic symptoms, and 41 per cent had no symptoms—the same percentages that were found in the total community group.

PHYSICAL FUNCTION RATINGS

Because of the importance of physical health in older people, a method was developed for rating the functional physical status of each subject. This was based in part on the extensive medical history, and on the results of physical and neurologic examinations and laboratory studies. The six possible ratings (from 0 to 5) on this scale are shown in Table 1.

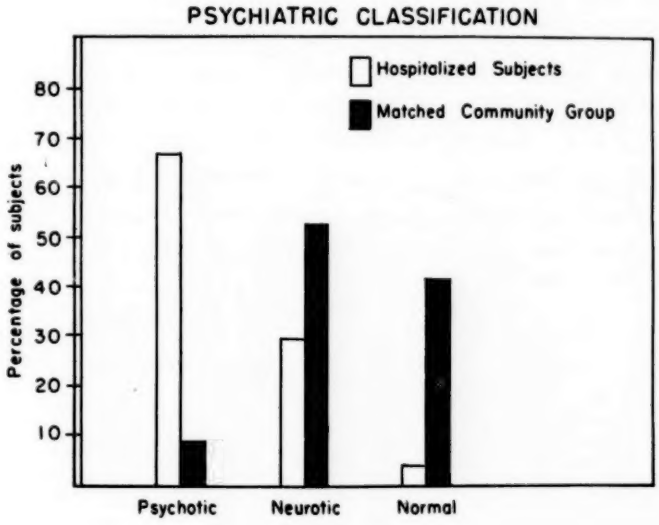


FIGURE 1

TABLE 1

Physical Function Ratings

0 =	No pathologic condition or disability
1 =	Disease diagnosed, but no limitation of social or industrial function
2 =	Limitation 20% or less
3 =	Limitation 20% to 50%
4 =	Limitation 50% to 80%
5 =	Limitation 80% to 100%

This scale is modified and adapted from those in use by the United States Army and Veterans Administration for rating disability. For our purposes, social limitation is defined as any restriction upon activity or communication involved in ordinarily possible social activities for the particular subject. Sometimes a hypothetically "normal" situation is reinforced by specific information regarding the subject's daily activity, *e.g.*, arthritic limitation of movement severe enough to prevent the subject from pursuing usual interests at church and at civic clubs but still permitting enjoyment of social intercourse with visiting friends would be rated 30 to 50 per cent social incapacity. On the other hand, limitation of vision and hearing to the point where understandable social relationships with others were practically terminated, would be rated a complete incapacitation.

When assessing industrial capacity, we included useful occupations (whether performed for pay or not), since most of our subjects were retired. For example, a subject with arthritis who could not possibly get to a place of work or to a part-time hobby activity if located outside the home was rated as seriously disabled. If, in spite of this limitation, he was able to engage in productive work around the home, he was not considered as being completely disabled. It should be noted that psychiatric limitations on ability to perform were not considered in conjunction with this rating. Only the physical aspects of the subject's potentiality for social and industrial activity were considered.

As indicated by the percentages in Figure 2, only 17 of the hospitalized group had either no pathologic lesion or a lesion without disability; 32 had some disability accompanying their physical problems. Thirty-five of the community group had either no disease or no disability therefrom, and 30 had some degree of disability. Thus, the hospital group has significantly more disability than the matched socio-economic group of the community subjects.

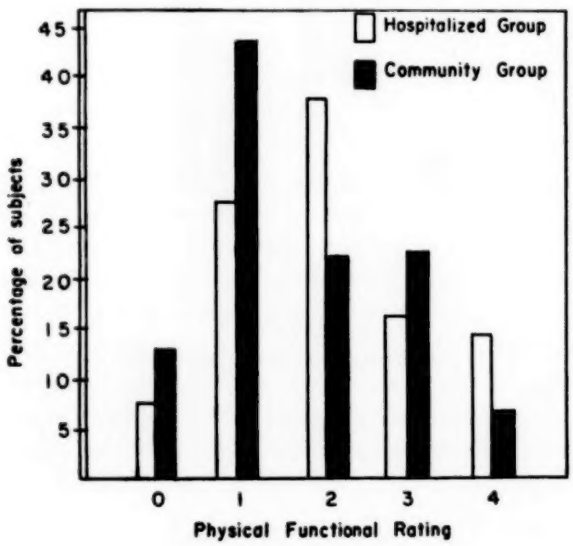


FIGURE 2

DISEASE PATTERNS

The entire community group suffered predominantly from loss of sight and hearing, arteriosclerosis, elevated blood pressure, pulmonary disease, arthritis, and limitation of movement in the joints. Physical function ratings were significantly reduced in the lower socio-economic group and in the older members of each group. Although the patterns of disease did not differ between socio-economic and other groups, the frequency of disease did, as indicated in Table 2.

When the hospital subjects were compared to the matched community subjects, however, there was a distinct difference in disease patterns. It should be noted that many of these conditions (for example, diminished olfactory sensation) would not enter into ratings of physical function.

One of the prominent differences was that in the pattern of the electroencephalogram (EEG). It can be seen in Figure 3 that there was a significantly higher number of generalized abnormalities (slow records) in the hospitalized subjects and a significantly higher number of specific abnormalities in the community subjects. The latter finding is explained largely by the frequency of temporal foci in community people.

Further confirmation of the trend toward a slowing of the EEG waves in the

TABLE 2

Conditions Appearing More Frequently in Lower Socio-Economic Group

Impairment of vision	($P < .001$)	
Arteriosclerosis	($P < .05$)	
Cardiovascular disease	($P < .05$) especially 70+ age group	($P < .05$)
High systolic blood pressure	($P < .05$) especially 70+ age group	($P < .02$)
High diastolic blood pressure	($P < .02$) especially 70+ age group	($P < .01$)
Pulmonary disease	($P < .02$) especially 70+ age group	($P < .05$)
Joints; limitation due to arthritis	Trend only	

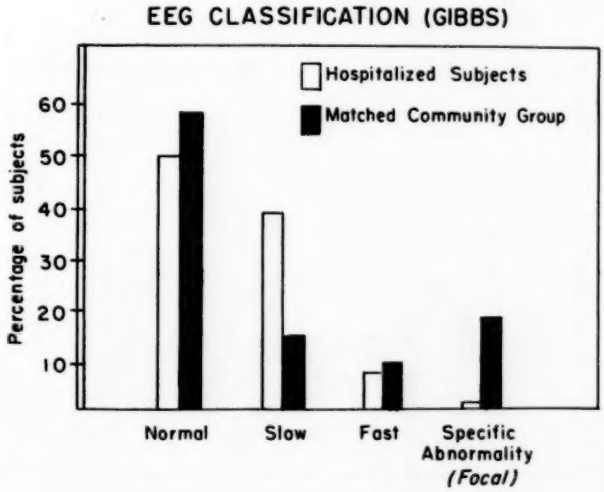


FIGURE 3

hospital subjects can be seen in Figure 4, showing the dominant EEG frequency. Only 2 subjects of the matched community group had records in which the dominant frequency was below 8 per second, whereas 33 of the hospital group had such records.

Because of the clear differences in EEG pattern, special attention was given to the neurologic findings in the two groups. Unfortunately, our program of complete auditory and visual examinations was focused on the community subjects, so the data are not comparable in the two groups. As Figure 5 indicates, diminution of vibratory sense and diminished olfactory sensation reached statistical significance. A clinical estimate was made concerning the origin of abnormal

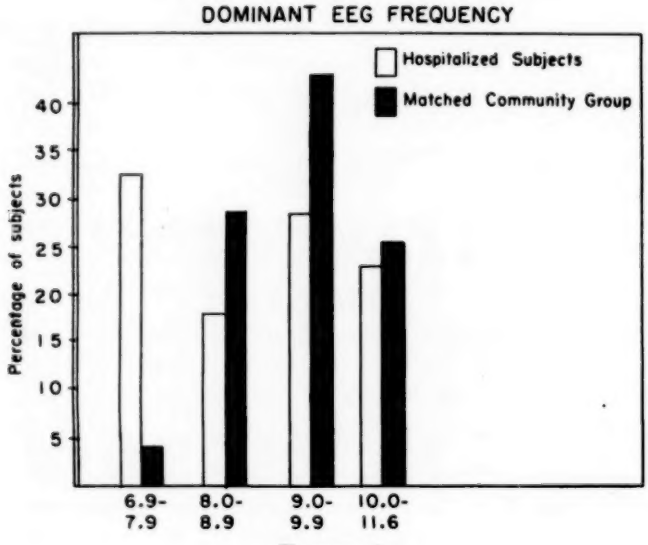
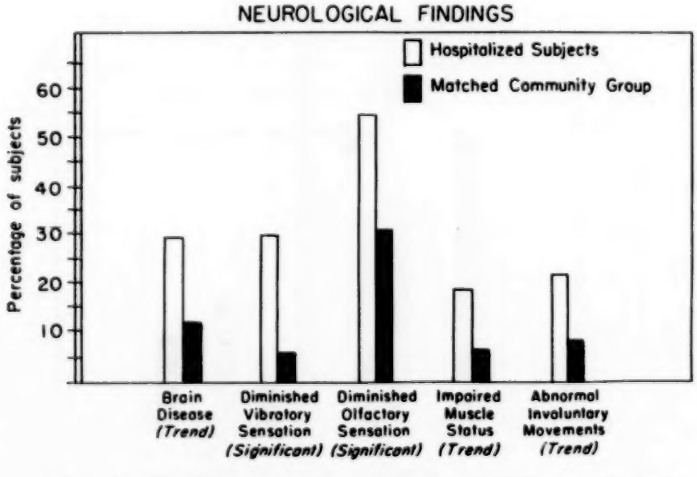


FIGURE 4



No significant differences in gait, associated movements, or reflex activity.

FIGURE 5

neurologic manifestations. Abnormal signs thought to have their origin in the cortex, cerebellum, brainstem or basal ganglia were recorded as indicating possible brain disease. Reduction in vibratory sensation was invariably confined to the lower extremities. Diminution of olfactory sensation was judged by the presence of, or correctness of, responses to four distinct odors. Tonus and strength of muscles were estimated in relation to age. Abnormal involuntary movements consisted of various tremors.

One of the prominent abnormalities in the community group was elevation of both systolic and diastolic blood pressure. Here again, a significant difference was found between the hospital subjects and the matched community group. As seen in Figure 6, both diastolic and systolic blood pressure tended to be more normal in the hospital group.

Another difference between hospitalized and community subjects was in their general nutritional status as evaluated clinically. In Figure 7 it can be seen that only 2 per cent of the community subjects were poorly nourished whereas 23 per cent of the hospitalized subjects were so classified. Community subjects tended to be more obese.

Differences between the hospital and community groups with regard to other diseases are summarized in Figure 8. The incidences of arthritis and limitation of joint movement were significantly higher in the community group, and there was a trend toward more peripheral venous disease and pulmonary disease. All types of arthritis were considered in the ratings, including rheumatoid, osteo-, gouty and traumatic forms. Peripheral venous disease included both thrombophlebitis and varicose veins. Pulmonary disease included asthma and emphysema.

There was virtually no difference between the two groups with regard to the incidence of cardiovascular disease, history of cardiac failure, or the presence of peripheral arterial disease.

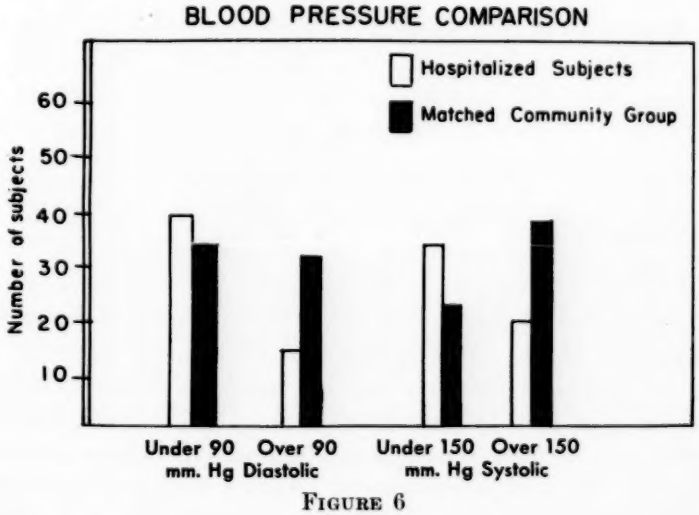


FIGURE 6

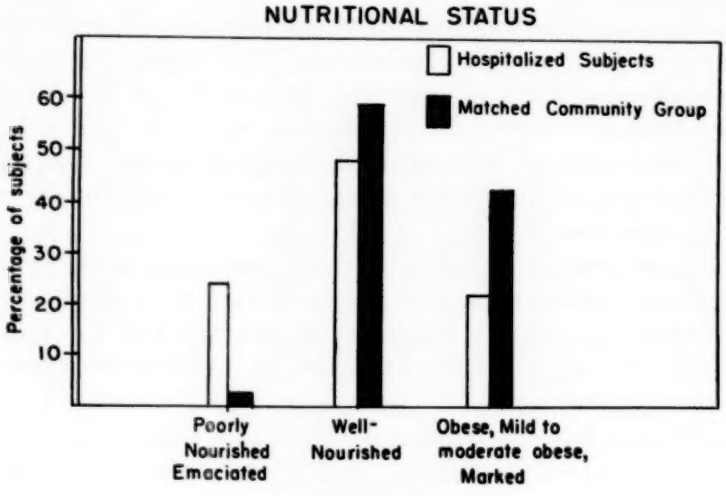


FIGURE 7

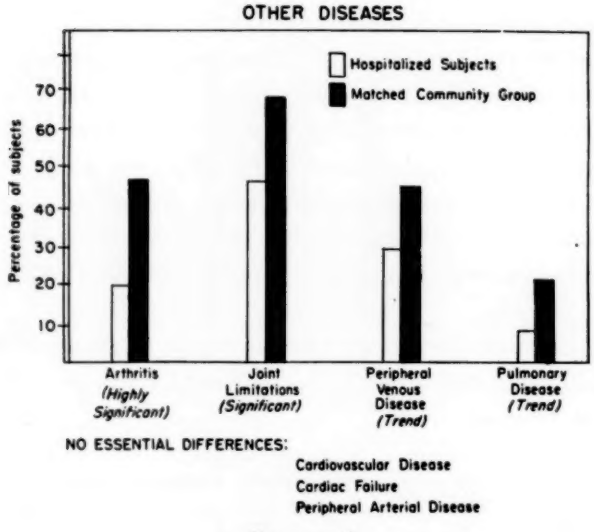


FIGURE 8

DISCUSSION

The clinical impression that subjects hospitalized because of psychiatric illness have greater limitations of physical function was confirmed by the data of the present study. Although the influence of age, sex, race and educational level could be eliminated by matching the subjects, the socio-economic condition could not be controlled at the level of occupational rating because of the prevalence of farmers in the hospital sample. Another factor possibly influencing the differences in physical function was the selection of the hospital subjects, not by age alone, but also by the criterion that they could communicate and cooperate sufficiently well for purposes of the research examinations. It may be that subjects with physical limitations in addition to psychiatric problems are admitted to the hospital before their ability to communicate deteriorates greatly.

A more likely possibility is that the marked difference in the pattern of disease incidence in this group indicates that specific disease conditions contribute to the hospitalization for psychiatric reasons. Supporting evidence is provided by the fact that the diseases with the highest incidence among the hospital patients were those involving neurologic status.

An increase in the incidence of slow-wave EEG abnormalities in hospital subjects has been noted by several authors (3–7). This kind of abnormality is not uncommon in association with senile and arteriosclerotic psychoses. Focal abnormalities, especially in the left temporal area, are demonstrably related to age and are of common occurrence in functioning community groups (3, 8).

A relationship between lowering of the blood pressure and slowing of the EEG waves has been reported by Obrist and co-workers (5, 9). In our series, the greater frequency of normal blood pressure in the hospital patients may have been a reflection of this tendency, especially since this group was part of Obrist's overall sample of hospitalized subjects. As he has pointed out, the slow waves in the EEG may be caused by reduction of the oxygen supply to the brain in persons whose cerebral vasculature is arteriosclerotic and whose blood pressure does not compensate for changes in the vascular bed.

Unfortunately the exacting examinations for auditory and visual functioning that were undertaken in the community subjects were not possible in the hospitalized subjects. Olfactory and vibratory sensations were markedly reduced in the hospitalized group. This finding suggests that a reduction in sensory stimulation plays a part in the origin of psychiatric problems. However, this was not determined by special testing, so the question remains open.

It is noteworthy that the hospitalized subjects did *not* exhibit a different pattern of incidence of vascular disorders other than peripheral venous disease. In spite of obvious severity in the organic mental disorder there was no increase in the incidence or estimated severity of generalized arteriosclerosis.

SUMMARY

Matched groups of 65 psychiatrically hospitalized patients and 65 actively functioning community subjects were compared. The hospital group exhibited significantly greater physical incapacity than did the community group.

Associated with this difference in physical functional capacity there was a different pattern of disease incidence in the hospitalized patients, manifested as follows: 1) slow, diffuse EEG waves were more frequent, and focal abnormalities were less frequent; 2) both systolic and diastolic blood pressures were more normal; 3) brain disease and sensory impairment were more frequent; 4) the nutritional status indicated more malnourishment and less obesity; 5) arthritis, limitations of joint movements, pulmonary disease and peripheral venous disease were less frequent. However, there was virtually no difference in the incidence of cardiovascular disease between the two groups of subjects.

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CORRELATION OF CLINICAL AND EXPERIMENTAL EFFECTS OF ANTIBIOTIC THERAPY FOR MASSIVE INTESTINAL INFARCTION SECONDARY TO ACUTE MESENTERIC VASCULAR OCCLUSION

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Occlusion of the superior mesenteric blood vessels is a major abdominal catastrophe. In the last two decades doctors have become sufficiently aware of this condition to make a diagnosis before the death of the patient. Though treatment, mainly surgical, has progressed, it leaves much to be desired. The over-all mortality is well above 75 per cent. It was our aim in carrying out this research project to correlate the experimental and clinical material on the subject.

ANATOMY

The superior mesenteric artery is a visceral branch of the abdominal aorta and supplies the entire bowel from the terminal duodenum to the midtransverse colon. It arises from the abdominal aorta about 1.5 cm. below the celiac axis and runs in an oblique manner between the layers of the mesentery to the right iliac fossa, where it terminates by anastomosing with one of its own branches, the ileocolic artery. (Just to the right, throughout its course, lies the superior mesenteric vein.) The branches of the ileocolic artery include: 1) the inferior pancreaticoduodenal, 2) from twelve to fifteen intestinal branches supplying the jejunum and ileum, 3) the middle colic, which arises from the upper portion and supplies the transverse colon; it divides into right and left branches which anastomose with the right and left colic arteries, 4) the right colic, which arises from the midportion of the artery and supplies the ascending colon; it divides into ascending and descending branches to anastomose with the middle colic and ileocolic arteries respectively, and 5) the ileocolic, the lowest branch, which supplies the cecum, appendix and terminal ileum; it divides into a superior and inferior branch which anastomose with the right colic and terminal portion of the superior mesenteric artery respectively.

The branches of the superior mesenteric vein correspond to those of the artery; the vein ends by joining the splenic vein to form the portal vein (1, 2).

CLINICAL PICTURE

Although it is extremely difficult to make the diagnosis of acute mesenteric vascular occlusion and differentiate between arterial and venous occlusion, some

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† Senior Medical Students; Summer Research Project.

authors believe that a preoperative diagnosis can be made (3, 4). As, for example, gastric ulcer differs from duodenal ulcer, so does occlusion of the superior mesenteric artery differ from occlusion of the superior mesenteric vein. The following are the important distinctions:

Vein	*Artery*
1. Slow onset.	1. Sudden onset.
2. Colicky pain that increases in severity as time progresses.	2. Violent and extreme abdominal pain.
3. Hematemesis and melena appear early due to intestinal congestion.	3. Melena and hematemesis appear later, usually with onset of gangrene.
4. Minimal leukocytosis.	4. More pronounced leukocytosis. —up to 40,000 WBC per cu. mm.
5. Normal or decreased blood pressure.	5. Shock and diaphoresis.

It has been noted by Wangensteen (5) that the patient with arterial obstruction may improve after the initial onset of abdominal pain; thus the physician may become lax and wait rather than prepare the patient for surgery as soon as possible. In the late stages, the symptoms of tenderness, rigidity, distention and fever are common to both forms of occlusion. Shock may appear early or late in the disease. When it is one of the presenting symptoms, usually the occlusion is large and there is reflex vasomotor collapse. When shock occurs late, it is usually secondary to the dehydration and hypovolemia produced by copious vomiting and diarrhea. In both cases the abdomen is as "silent as the grave."

In spite of these differentiating factors, most often the diagnosis is made at operation. In the early stages of acute arterial occlusion, the surgeon may see a bowel that appears completely normal, and consequently the evidence provided by the absence of pulsations in the mesentery may be easily overlooked. Therefore, in the surgical exploration of an acute abdominal condition, it is wise to palpate the mesenteric artery. The bowel may be grey-white and contracted, with variable intestinal activity and arterial pulsations. In the later stages, the surgeon will find bloody peritoneal fluid, and the alterations in color that are associated with gangrenous necrosis. At this stage the prognosis is extremely poor.

Early occlusion of the superior mesenteric vein presents a picture of a bowel which is dilated, edematous, cyanotic and congested, and a blood-filled abdomen and intestinal lumen with petechiae and ecchymotic areas on the mesentery. Later, the gangrenous process becomes apparent; at this point differentiation cannot be made (6).

INCIDENCE AND ETIOLOGY

Although the incidences of venous and arterial occlusions vary with each

series, they appear to be approximately equal according to Campbell and Mears (3):

Authors	Total Number	Arterial	Venous	Combined or Undiagnosed
Jenson & Smith	51	29	12	10
Whittaker & Pemberton	60	19	27	14
Uricchio, Calenda, & Freedman	1,142	50%	44%	6%

The incidence of *mesenteric* vascular occlusions ranges from 0.01 to 0.1 per cent, this low incidence probably being the only consolation in the entire problem.

The etiology of arterial and venous occlusion varies widely. In arterial occlusion, cardiac disease plays the predominant role. Emboli from vegetations on cardiac valves, mural thrombi, and atheromatous aortic plaques (as found in rheumatic and coronary heart disease) cause 60–80 per cent of all mesenteric occlusions. Mesenteric atherosclerosis as part of generalized arteriosclerosis is a frequent finding. Rarer etiologic conditions are periarteritis nodosa, Raynaud's disease, malnutrition and trauma—the latter especially after surgical exploration of the abdomen. Aneurysms, whether they be aortic or mesenteric, occasionally cause occlusion. Distention of the intestinal tract, as found in mechanical obstruction, may result in mesenteric arterial occlusion. There are also idiopathic cases.

Eighty per cent of mesenteric venous occlusions are secondary to other pathologic conditions in the abdomen, especially those of the portal system. Appendicitis, pyleophlebitis, ulcerative colitis, liver disease producing portal stasis and hypertension, operative procedures in the abdomen especially splenectomy, and extra-portal pressure produced by tumors and polycythemia are among the most common; then there are the spontaneous thrombotic occlusions (3, 6, 7).

PATHOLOGIC PHYSIOLOGY

When a mesenteric artery becomes acutely occluded, a reflex spasm affects the distal vessels and initially causes expulsion of the blood. The venous system is emptied and, since no arterial blood enters, the bowel wall contracts and turns greyish white. After this initial phase, the spasm ceases and vasodilatation occurs in association with some venous backflow. Within the next six to twelve hours, anoxia of the intestinal tissues produces necrosis, edema, and changes in temperature and color. Peristalsis ceases, fluid and gas accumulate within the lumen of the bowel, and distention ensues. The bowel wall becomes thin, and bacterial invasion begins. With the onset of gangrene, perforation and peritonitis occur, followed by death (7).

TREATMENT

The present treatment of acute mesenteric vascular occlusion is surgical and the type of operation is dependent on whether the etiologic agent is an embolus

or a thrombus. A past history of cardiac disease such as myocardial infarction, rheumatic fever with atrial fibrillation, or changes in rhythmicity of the heart and a recent history of episodes of transient hemiparesis, paresthesias or slurred speech, with sudden development of the picture of acute mesenteric arterial occlusion, point to an embolus as the etiologic factor. The treatment of choice is a mesenteric embolectomy when the case is recognized early enough (twelve to sixteen hours). If the surgeon is sure the bowel is viable at this time, there is no need for further exploration of the abdomen. If there is doubt, the abdomen should be re-opened to determine viability. If irreversible changes have occurred, the necrotic segment should be excised. Embolectomy is far superior to excision because, when the infarction is large, it offers the patient a good chance of leading a normal life, whereas extensive resection will result in a gastro-intestinal cripple if the patient survives. Ancillary therapeutic measures are vasodilators, splanchnic nerve blocks, procaine infiltration of the mesentery, antispasmodics, anticoagulants, antibiotics, and proper nutrition (8–10).

For treatment of thrombotic vascular occlusion, the procedure of choice is excision of the involved segments followed by end-to-end anastomosis when feasible. The bowel may be brought to the exterior when viability is doubtful (5).

REVIEW OF LITERATURE

In the last fifteen years, research workers have been interested in antibiotic therapy for intestinal infarction. Sarnoff and Fine (11) showed that the use of succinylsulfathiazole (sulfasuxidine) postoperatively for various periods of time caused a definite decrease in the mortality rate among dogs in which they had produced venous occlusion in 50 centimeters of ileum:

Animal Group	Treatment	Mortality Rate	Incidence of Perforation
1	None	87%	75%
2	Intraluminal sulfasuxidine at time of operation	66%	0
3	Intravenous sulfasuxidine for 1–2 days postop.	50%	0
4	Sulfasuxidine preop. and postop.	25%	0

By carrying out blood volume determinations in the controls as well as in the experimental dogs, they showed that there were no significant alterations in the two groups and that death could not be attributed to shock resulting from blood loss secondary to vascular damage. These results suggested that: 1) chemotherapy has a distinct advantage in mesenteric vascular occlusion and sustains the animal until collateral circulation appears; this was shown by histologic sections twenty to thirty days postoperatively, in which the damaged bowel wall was indistinguishable from the normal bowel wall; and 2) death as a rule is due to secondary infection through a permeable bowel wall and not due to shock secondary to blood loss (11).

Harper and Blain (12, 13) performed similar work, using isolated loops of ileum and giving penicillin parenterally or intraluminally. They had two groups

of dogs—one not treated and the other treated. In the untreated group the mortality was 100 per cent, with no animal surviving more than six days; 87 per cent died within three and a half days. In the group treated with penicillin intraluminally 100 per cent lived more than nine days, 93 per cent for over thirteen days, and 60 per cent for over one month. In the parenterally treated group, 100 per cent lived more than eighteen days. By adding the factor of occlusion of the bowel lumen as well as venous return and thus simulating intestinal obstruction in man, Harper and Blain almost tripled the survival time and obtained 4 cures out of 13 cases. All of their animals were treated symptomatically in order to eliminate shock as a cause of death (14–16). Poth and McClure (17) carried out similar studies, except that they ligated the vessels first individually and then together, and administered sulfasuxidine and sulfathalidine preoperatively and postoperatively. There was a marked decrease in mortality rate among their treated animals:

Group	Mortality Rate (%)		
	Venous ligation	Arterial ligation	Both
Untreated	95	50	64
Treated	27	9	9

The efficacy of antibiotics appears to reside in their ability to alter and reduce the intestinal flora and thereby to reduce invasion of the bowel wall by bacteria or their derivatives. Otherwise these bacterial products cause thromboses of the vasculature, especially at the capillary and arteriolar level, and thereby prevent the formation of collateral circulation.

EXPERIMENTAL WORK OF PRESENT STUDY

Mongrel dogs were used, without specification as to size, type or age. They were alternately labeled control and experimental, with random sampling. Each animal was anesthetized with sodium Nembutal, 1.0 ml. per 5 pounds of body weight. A vertical incision was made from the xiphoid process caudally, and the layers of the abdominal wall opened. The superior mesenteric artery was located by lifting the transverse colon and securing the root of the mesentery. The posterior parietal peritoneum was incised, the mesenteric fat dissected, and the vessels exposed. Once completely exposed, the artery was ligated with 4–0 silk ligatures doubled-over proximal to the first branch. A second ligature was used at a site distal to this point. A sclerosing solution of 50 per cent glucose was injected into the distal portion of the artery. The abdomen was then closed. The animals received 1,000,000 units of Combiotic (penicillin and dihydrostreptomycin) after operation, and for seven days thereafter. The control dogs were untreated. In the treated dogs which survived, the abdomen was re-opened seven to nine days afterward, to determine the condition of the bowel and the state of the collateral circulation. This was accomplished by sacrificing the animal, cannulat-

TABLE 1

Collateral Circulation in Dogs with Experimental Occlusion of Superior Mesenteric Artery

Dog No.	Experimental Group, Treated with Combiotic	Control Group (No Treatment)	Survival Time
1		X	24 hours
2	X		7 days
3		X	24 hours
4	X		7 days
5	X		24 hours
6	X		7 days
7	X		8 days
8		X	24 hours
9		X	48 hours
10		X	7 days
11		X	24 hours
12	X		24 hours
13	X		9 days
14		X	12 hours
15	X		3 days (distemper)
16		X	12 hours
17	X		2 days (distemper)
18	X		6 days
19	X		2 days
20	X		8 days
21	X		8 days
22	X		8 days
23		X	48 hours

ing the thoracic aorta and injecting methylene blue. Any collateral vessels would promptly fill with the dye.

The important difference between our work and previous work on antibiotic therapy for intestinal infarction is that: 1) our experiment more closely duplicated mesenteric vascular occlusion as it occurs in man, 2) we produced massive infarction of the entire small bowel and part of the large bowel as compared to infarction in small isolated segments produced by other workers, and 3) there was complete lack of adequate collateral circulation in association with the complete acute occlusion, and therefore antibiotic therapy was the essential factor in maintaining the lives of the experimental animals.

From the data in Table 1, it may be seen that 8 of the 9 controls died within twenty-four to forty-eight hours—a survival rate of only 10 per cent. In the experimental group, 9 of 12 animals‡ survived six days or more—a survival rate of 75 per cent.

Antibiotic therapy apparently acts on the intestinal flora to prevent bacterial products, enzymatic substances or necrotic tissue from producing thrombosis of the intramural blood vessels, and thereby permits the formation of collateral circulation (17). After injection of the thoracic aorta of the surviving animals,

‡ Exclusive of Dogs # 15 and # 17, which died in 3 and 2 days respectively, from distemper.

it was found that the main collateral blood supply came from the celiac and inferior mesenteric trunks traveling mainly through intramural channels. Previously, these channels had been considered inadequate because no one had seriously investigated the intramural anastomotic channels. Recently, Benjamin and Becker (18) showed the vast number of these channels, as well as their exact distribution and connection with each other. The vasa recta (which come off the intestinal arcades) bifurcate as they reach the mesenteric border of the small intestine. These bifurcated vessels penetrate the serosal and muscular layers of the bowel to reach the submucosa. In this submucous layer, the vasa recta anastomose throughout the length of the small bowel and form a longitudinal channel throughout the length of the organ in the area between the mesenteric and antimesenteric border. The vasa recta then continue around to the antimesenteric border and there anastomose with the vessels of the opposite side as well as adjacent vessels to form a second longitudinal channel which also runs the length of the small bowel. From this "vascular signet ring," vessels run in a perpendicular manner to the mucosa and muscularis (18–20).

CLINICAL CASE REPORTS

The following case reports are representative of the clinical problem under investigation:

Case 1

F. B., a male aged 66, entered the hospital on January 15, 1957, with mitral valvular disease, rheumatic heart disease (decompensated) and pulmonary congestion.

The preoperative diagnosis was mesenteric thrombosis, and the postoperative diagnosis was superior mesenteric artery thrombosis.

The abdomen was opened through a right paramedian incision, made under local anesthesia. The entire small intestine was a deep plum color, the mesentery was pale, and the superior mesenteric artery was pulseless. Numerous loops of small intestine exhibited greyish-white mottling. Because of extensive involvement from the ligament of Treitz to the ileocecal valve, resection was not attempted. The abdomen was closed in layers in the usual manner, using 2-0 cotton throughout.

The patient was treated with 1,000,000 units of penicillin daily, nasal oxygen, heparin, electrolytes intravenously, and gastric suction. He was discharged on February 4, 1957, able to eat a general diet.

Case 2

M. M., a female aged 71, was admitted on September 17, 1958. The preoperative diagnosis was acute mesenteric thrombosis on the basis of heart disease. The patient was anesthetized with intravenous pentothal sodium and the abdomen was opened. The superior mesenteric artery was pulseless, and the entire small intestine was plum colored, with the exception of the last 6 inches in the region of the ileocecal valve. Except for this 6-inch section, the entire small intestine was resected and an anastomosis was made between the distal segment of small intestine and the duodenum at the ligament of Treitz.

The patient was treated with heparin, nasal oxygen, electrolytes intravenously, and gastric suction. She died on September 23, six days after admission.

SUMMARY AND CONCLUSIONS

A review is presented of clinical and experimental data on occlusion of the superior mesenteric artery, and new data are reported regarding the efficacy of antibiotics in treating acute massive infarction of the bowel. Acute complete

mesenteric vascular occlusion was produced in dogs. The mortality rate in those treated with antibiotics was 25 per cent. In the survivors, re-exploration of the abdomen eight days later revealed a viable small intestine as compared to a gangrenous, perforated intestine in the control dogs, most of which died within twenty-four to forty-eight hours.

When mesenteric vascular occlusion has caused extensive necrosis of the intestine, antibiotic therapy should be used in conjunction with embolectomy, instead of attempting extensive resection of the bowel. The latter leads to gastro-intestinal crippling and involves a high mortality rate.

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EFFECT OF MASSIVE DOSES OF PENICILLIN ON AGING PATIENTS WITH GENERAL PARESIS

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This study of the effect of prolonged therapy with massive doses of penicillin on aging patients suffering from long-standing general paresis (1–7) was undertaken in order to assess particularly the serologic changes.

METHODS AND RESULTS

Thirty-five patients between 40 and 77 years old were treated over a period of six years with massive doses of penicillin and procaine penicillin (Duracillin), ranging from 15 million to 84 million units. Many of those patients had been receiving malaria therapy prior to the institution of penicillin. The routine procedure was to perform a spinal tap, and then administer a course of 25 million units of penicillin. Most patients received 600,000 units of penicillin daily for forty-two days, but some received it on alternating days as it was felt that the prolonged administration might improve the therapeutic results. Approximately six months following the last injection of penicillin, the serologic tests were repeated. If the results were still positive, more penicillin was administered. Six patients were treated with penicillin only, in dosages ranging from 19 million to 80 million units. One received penicillin under the auspices of the National Research Council in 1945.

In all patients who were treated exclusively with penicillin, the Wassermann reaction remained positive. Twenty-nine patients received malaria therapy first; in 7 of these, the results of the Wassermann test became negative. Two of the 22 patients who retained their positive reactions to the Wassermann test were not further treated. The other 20 received penicillin therapy later in doses ranging from 15 million to 84 million units. In 16 of these patients the Wassermann reaction remained positive, but in the other 4 it became negative as a result of combined malaria-penicillin therapy. The following case is representative:

J. R., a 40-year-old man, was admitted with general paresis in 1948. The result of a Wassermann test on spinal fluid was 4 plus (blood, positive); Ross, 3 plus; Pandy, 3 plus; cell count, 14; gold curve, 5543332110; and protein content, 55.5 mg. per 100 ml. The patient received a course of malaria therapy in January 1949. In March 1949 the spinal fluid Wassermann reaction was 4 plus (blood, positive); and the protein content was 38.4 mg. per 100 ml. In April 1955 the spinal fluid Wassermann reaction was 1 plus; cell count, 3; and gold curve, 2111100000.

The patient received 25 million units of penicillin. In March 1957 the spinal fluid Wassermann reaction was positive; cell count, 8; and protein content, 53 mg. per 100 ml.

Another course of 25 million units of penicillin was given between March and April 1957. In June 1958 the spinal fluid Wassermann reaction was still positive; Ross, 1 plus; Pandy, 1 plus; gold curve, 2211100000; and protein content, 36.4 mg. per 100 ml.

In June 1958 the patient received another course of 25 million units of penicillin. In April

1959 the serologic tests were repeated. The spinal fluid Wassermann reaction was now negative (blood, positive); Ross, negative; Pandy, negative; cell count, 3; and gold curve, 0111100000.

A dose of 9 million units of penicillin was given on May 15, 1959. Serologic tests were repeated on January 11, 1960. Both spinal fluid and blood Wassermann findings were negative, the blood Mazzini reaction was doubtful, and the gold curve was flat.

The total amount of penicillin given was 84 million units.

J. R. is now an amiable, well-behaved patient who gets along well and is able to take care of himself on the ward. He is in poor contact with his environment and does not know his age, nor the month or year. He has no delusions or hallucinations. His speech is slurred and a peri-oral tremor is present. Epileptic seizures, which were not controlled by administration of primidone (Mysoline) and diphenylhydantoin (Dilantin) disappeared following the last administration of penicillin.

COMMENT

It is noteworthy that in all the patients treated with penicillin exclusively, the Wassermann reaction remained positive, whereas in 7 of the patients treated with malaria and in 11 of those treated with both malaria and penicillin the Wassermann findings became negative. These results seem to support the observations of Orban and Lazarowitz (4) that combined malaria-penicillin therapy is superior to either malaria or penicillin alone for reversal of positive Wassermann findings.

A comparison of today's hospital admissions for central-nervous-system syphilis with those of several years ago shows a pronounced decrease in the primary and secondary forms of syphilis that develop into the late forms, especially tabes dorsalis. However, the number of older patients being admitted with late syphilis is still large. The question arises whether these cases are due to failure of treatment before the days of penicillin or due to failure of penicillin therapy. The findings in penicillin-treated cases indicate that the ineffectiveness of this agent in producing negative results with the Wassermann test is at least partly the cause of the continuing high admission rate of paretic patients to mental hospitals.

In our series, no convulsions, Jarisch-Herxheimer reactions, or other forms of allergy were noted within forty-eight hours following administration of penicillin. A probable Jarisch-Herxheimer reaction in penicillin-treated cases of neurosyphilis was noted by Tucker and Robinson (7). In some patients whose seizures were not well controlled by anticonvulsants, the number and intensity of the attacks decreased following administration of penicillin.

CONCLUSION

The results of this study on 35 aging patients with long-standing general paresis support the findings of certain other workers that combined treatment with malaria and massive doses of penicillin is more effective than either malaria or penicillin alone in reversing positive serologic reactions for syphilis.

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BOWEL HYGIENE IN THE GYNECOLOGIC GERIATRIC PATIENT

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Poor bowel hygiene leading to obstipation and fecal impaction is a serious problem to both the geriatric patient and the nurse. The routine use of strong cathartics and enemas in many hospitals is unphysiologic. In this study, a combination of dioctyl sodium sulfosuccinate with anthraquinone derivatives of cascara (Peri-Colace)[1] was used in a series of elderly gynecologic patients in the management of constipation and the prevention of fecal impaction.

THE PROBLEM

Good health and mental attitude are influenced significantly by the regularity of the bowels. The bowel movement is an important event in the day of an elderly person; when it is missed, it is a matter of considerable concern. Lack of attention to this regularity frequently leads to severe discomfort for the patient.

Old people lead inactive and sedentary lives. This factor, combined with general debility and a low-residue diet, makes them predisposed to obstinate constipation and fecal impaction (1). The abdominal muscles in geriatric patients are weakened; when this condition is coupled with cardiovascular and degenerative neurologic diseases, the patient often does not have enough strength to effect a bowel movement. Only temporary relief is afforded by repeated enemas, and cathartics often require increased dosage to be effective.

Fecal impaction is often discovered during vaginal examination. Then the completion of the gynecologic examination has to be deferred until the fecal material can be eliminated from the bowel. The feces may be palpated as high as the sigmoid and lower colon, making it almost impossible to determine the status of the genitalia. Our experience has been similar to that of Dresen and Kratzer (2), who reported that 98 per cent of fecal impactions occur in the rectum.

Impactions place an added burden on an already overworked nursing staff. Bed linens must be changed frequently because of seepage from the rectum, and the patient has to be bathed. The necessary enemas are unpleasant for both the nurse and the patient. Elderly patients are often mentally confused and unclean in their personal hygiene, adding to the difficulty. Therefore, every effort should be directed to preventing impactions.

Prior to the advent of the fecal softening agents, mineral oil was commonly used as a lubricant to prevent impaction. However, there is ample evidence that mineral oil is not a harmless substance, as was once believed (3). Mineral oil interferes with the absorption of the fat-soluble vitamins, interferes with di-

[1] Kindly supplied by Mead Johnson & Company, Evansville, Ind.

gestion, may contain carcinogens, and as much as 60 per cent may be absorbed from the intestine. Leakage of oil from the rectum is also unpleasant.

Rosenfeld and associates (4) successfully used dioctyl sodium sulfosuccinate for the prevention of fecal impaction. This compound is not a laxative in the commonly accepted sense, but acts as a wetting agent; it emulsifies oil in the stool and prevents the absorption of fecal water. Thus the stool is maintained in a soft, easily-passed condition (5). However, Rosenfeld *et al.*, found that it was necessary to prescribe a peristaltic stimulant in addition to dioctyl sodium sulfosuccinate in order to evacuate these soft stools from the colon. This was especially true in patients with atonic constipation or physical weakness.

In our study, we used a combination drug (Peri-Colace), each capsule of which contained 100 mg. of dioctyl sodium sulfosuccinate and 30 mg. of Peristim (glycosides of cascara). Peristim is a mild peristaltic stimulant which acts through the blood stream directly on the colon. The value of Peri-Colace as a stool softener and peristaltic stimulant is well documented (1, 6–8).

THE STUDY

The 87 patients were on the Gynecological Service of the Bird S. Coler Hospital, New York, and all had a history of chronic constipation and repeated fecal impactions. They ranged in age from 55 to 89 years, the average being 68 years. Most of them had one or more established disorder in addition to the gynecologic complaint. These disease entities included cardiovascular conditions, diabetes, severe arthritis, multiple sclerosis, cancer, and advanced arteriosclerosis. Forty-seven of the patients were bedfast.

Some of the patients had received initial treatment with dioctyl sodium sulfosuccinate alone for periods of up to two weeks. This compound had effectively softened the stools, but evacuation was not always accomplished because of lack of peristalsis. Consequently, the medication was changed to Peri-Colace alone.

The initial dosage of Peri-Colace was 2 capsules daily for one week. Subsequently, the dosage was 2 capsules twice weekly for six to fourteen months. In several of the more difficult cases, 3 or even 4 capsules were given twice weekly.

TABLE 1

No. of Patients	Status	Results with Peri-Colace		
		Excellent	Good	Poor
1	Ambulatory	17	1	0
45	Semi-ambulatory	39*	5	0
25	Bedfast	19	6	0
Total 87		75	12	0

* One patient who had loose stools during Peri-Colace medication, had excellent results when treated with dioctyl sodium sulfosuccinate alone.

All patients continued to achieve adequate elimination, with only an occasional low enema required.

In this report the results are described as follows: Excellent: when no supplemental medication was required and elimination occurred at least every other day; most of the patients in this group had daily bowel movements. Good: when occasional rectal flushings were required as supplemental therapy. Poor: when the medication failed to produce regular bowel movements, and regular enemas and flushings were required.

The results are listed in Table 1. They were excellent in 75 of the 87 patients (86 per cent); good in 12; and poor in none. The medication was discontinued in 1 patient who had loose stools, but this case was managed successfully with dioctyl sodium sulfosuccinate alone.

COMMENT

Most of the patients received Peri-Colace for six to eight months, and some for more than one year. To date no patient has experienced further difficulty with fecal impaction. Griping, flatulence, rectal irritation, or other side-effects were not observed. The improved mental outlook and buoyed spirits of these patients suggest that Peri-Colace should be considered most favorably when dealing with the problems of bowel hygiene in the geriatric patient. Moreover, the nurses were most enthusiastic about the medication, since the need for enemas was infrequent and fecal impactions no longer developed.

SUMMARY

A combination of dioctyl sodium sulfosuccinate and glycosides of cascara (Peri-Colace) in capsule form proved to be an effective agent in the treatment of chronic constipation and fecal impaction in a series of 87 elderly gynecologic patients. No side-effects were observed. The improved bowel hygiene of these patients was reflected in their general mental outlook and physical condition.

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NORMAL QRS INTERVAL IN LEFT BUNDLE-BRANCH BLOCK. REVIEW OF THE LITERATURE AND PRESENTATION OF A CASE*

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It is almost fifty years since Lewis (1) first described intermittent bundle-branch block. White (2) stated that temporary or functional bundle-branch block is rare as compared to the permanent form. In 1938 Comeau, Hamilton and White (3) reported 13 cases of intermittent bundle-branch block and reviewed 58 cases up to that date. Vesell (4) emphasized the heart rate in relation to intermittent bundle-branch block; although he recognized the cardiac rate as a critical factor, he attributed intermittent block to underlying cardiac disease.

There are several reported instances of reversal to normal conduction some time after the onset of bundle-branch block. Digilio (5) reported reversal of left bundle-branch block to the normal conduction following correction of toxic goiter, and demonstrated a marked difference in rate before and after treatment. Spontaneous disappearance of left bundle-branch block of four years' duration in a 56-year-old soldier was reported by Kalett (6). Shearn and Rytand (7) made a study of 8 cases of intermittent left bundle-branch block and stated that this type of block probably represents a transitional stage before the development of permanent block. Gardberg and Rosen (8) restored normal conduction upon stimulation of the carotid sinus in a patient with an initial attack of left bundle-branch block but no evidence of heart disease. Lamb and associates (9) reported 2 cases of intermittent left bundle-branch block (one with arteriosclerotic heart disease and the other with myocardial infarction) in which the reconversion of left bundle-branch block to normal conduction follow the compensatory pause after premature ventricular contraction.

CASE REPORT AND ELECTROCARDIOGRAPHIC FINDINGS

The present report concerns a case of left bundle-branch block in which there was spontaneous temporary reversion to normal conduction, as confirmed by a normal QRS interval in the electrocardiogram.

A. D., a 60-year-old male white laborer, suffered ten days of anginal pain before admission to the hospital. X-ray examination showed a moderate amount of cardiac enlargement to both left and right, a tortuous aorta, and minimal congestion of the lungs. Other laboratory findings were noncontributory. Four electrocardiograms taken a week apart, showed left bundle-branch block. On the day of discharge the electrocardiogram showed normal conduction in all the twelve leads. The next day the electrocardiogram again showed prolongation in most of the leads.

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Figure 1 shows left bundle-branch block with a rate of 70–85 per minute. Figure 2 shows normal conduction in all the twelve leads of the electrocardiogram, with a rate of 80–84 in lead I, 68 in lead II, and 65–68 in lead III. Figure 3 shows left bundle-branch block in the first three rows, with a rate of 80 per minute; disappearance of the block is demonstrated in the V leads 1, 2 and 3, with rates of 75, 82 and 80 respectively. In V leads 4, 5 and 6 it is evident that the block has returned, with a rate of 80 per minute. The three tracings are presented with the standard leads accompanied by the augmented unipolar leads on the same strip, and all twelve leads on one chart (10).

Figure 4 shows the conversion of left bundle-branch block to normal con-

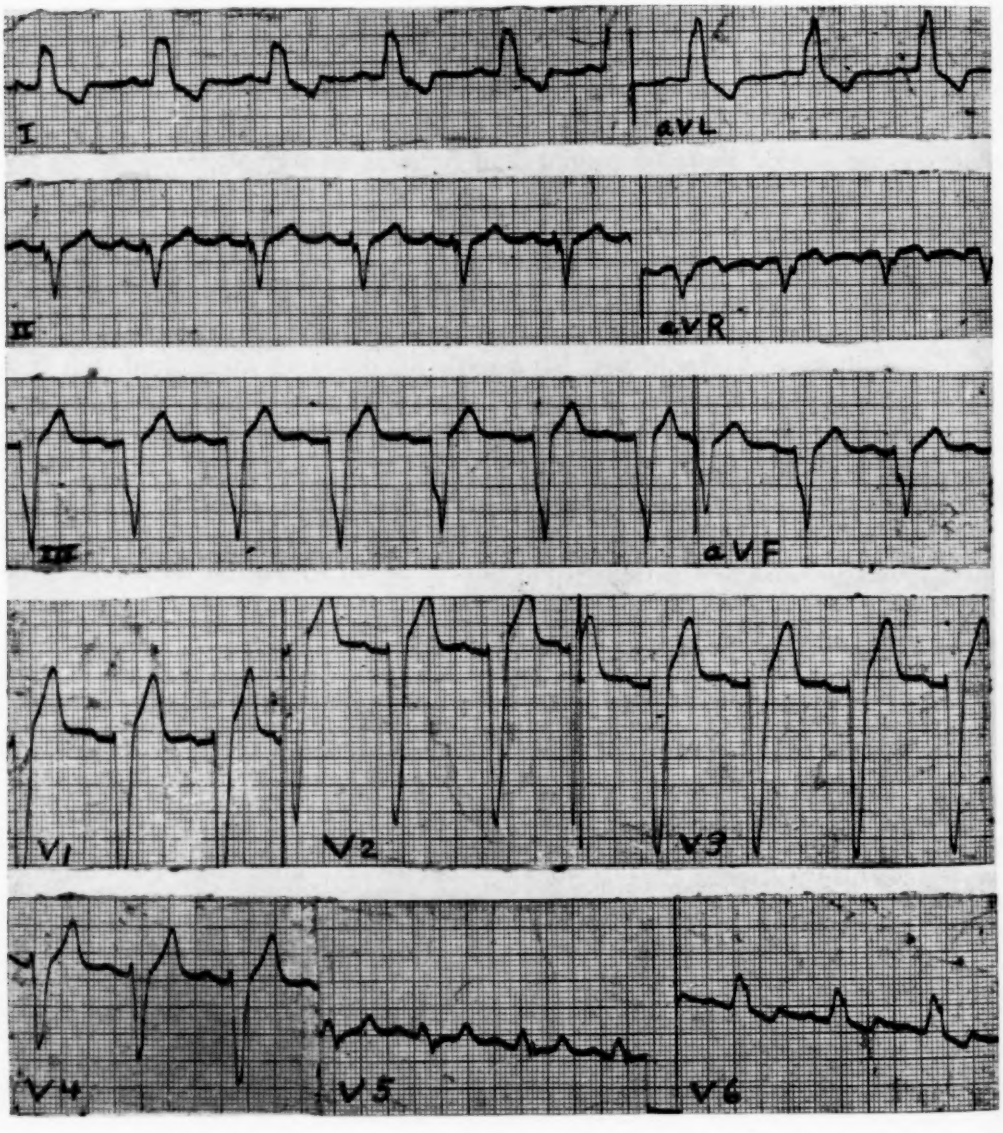

FIG. 1. Twelve-lead electrocardiogram showing left bundle-branch block with a rate of 70–85 per minute.

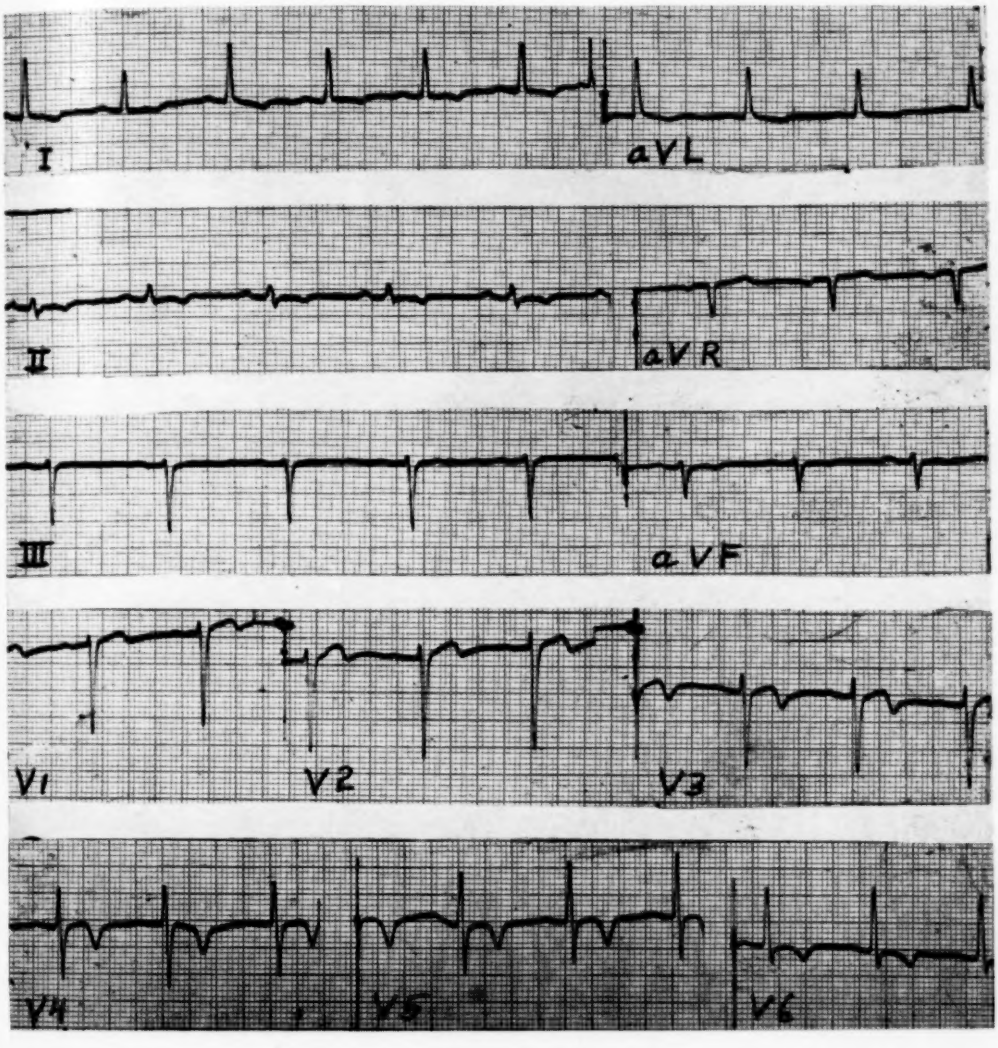

FIG. 2. Twelve-lead electrocardiogram showing normal QRS conduction with a variable rate of 80–84 in lead I, 68 in lead II, and 65–68 in lead III.

duction, and normal conduction back to bundle-branch block. The transition occurred spontaneously without any attempt at manipulation of the carotid sinus, hyperventilation, or change in body position. The R-R interval was uniform up to the time of the change from block to normal conduction, and the rate was 2 beats slower after the conversion. Normal conduction continued for half an hour and the rate increased to about 73 per minute. The last R-R interval before re-conversion to block was .04 second shorter than the previous cycles, with the rate increasing to 75 per minute after the block was re-established.

DISCUSSION

In the case presented here and in other forms of heart disease, left bundle-branch block may come and go, as demonstrated in the precordial leads of

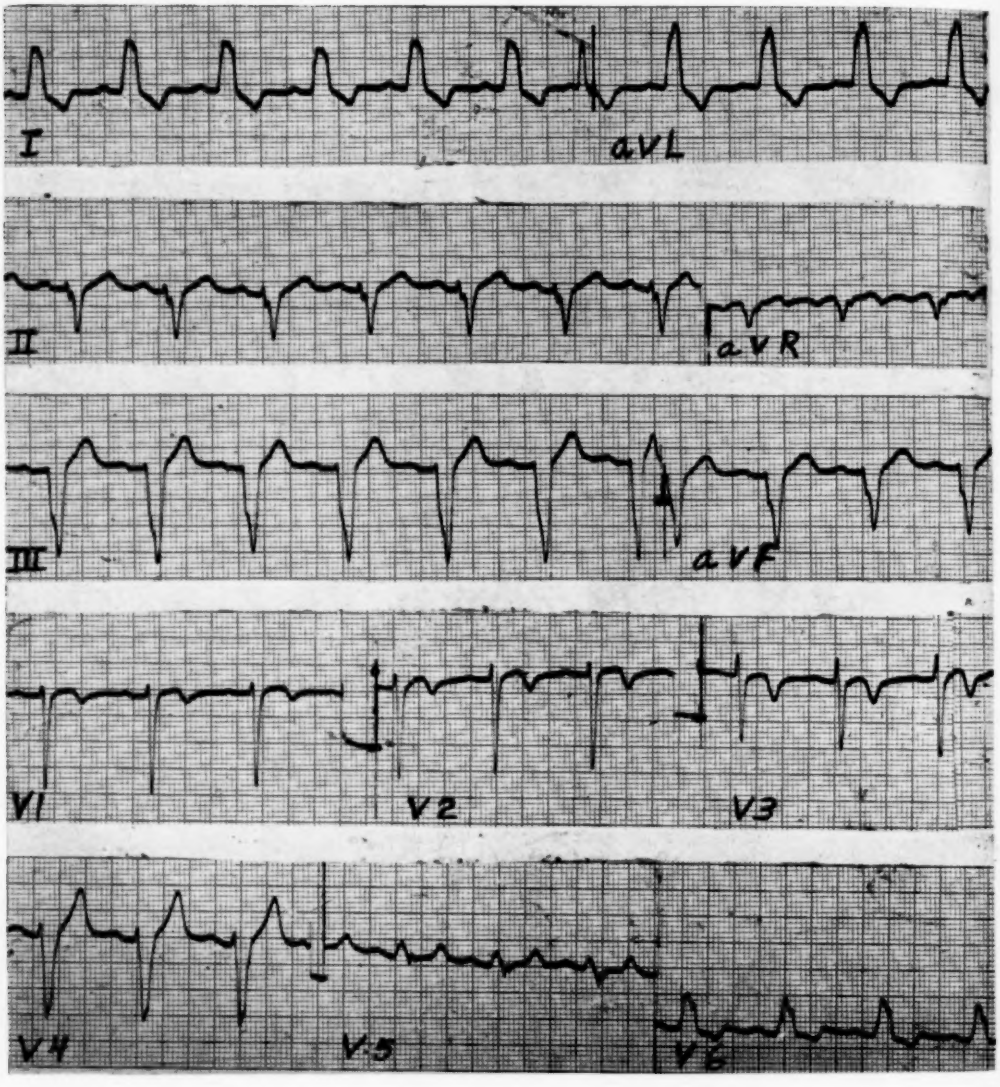

FIG. 3. Twelve-lead electrocardiogram showing left bundle-branch block in the first three rows, with a rate of 80 per minute. The signs of bundle-branch block are abolished in the V leads 1, 2 and 3 with a rate of 75, 82 and 82 per minute, respectively. The conduction defect has returned in the V leads 4, 5 and 6 with a rate of 80 per minute.

Figure 3, or may disappear completely, as demonstrated in Figure 2. This occurs because the conductivity of the bundle is depressed but not abolished. The bundle is able to conduct when the cycle length is long enough to allow for the increased time needed for the bundle to recover. Accordingly, bundle-branch block may appear when the rate is increased, and disappear when the rate is diminished. With only a small increase in the refractory period, the rate has to be quite rapid before left bundle-branch block appears.

Gardberg (11) states that once left bundle-branch block is abolished by slow-

FIG. 4. A single, continuous electrocardiogram with a rate of 65 per minute (top row) showing spontaneous conversion of left bundle-branch block to normal conduction without any compensatory pause; the rate after conversion is a beat or two slower. Normal conduction continued for half an hour, with the rate increasing to about 73 per minute. There was spontaneous return to bundle-branch block without any compensatory pause; the rate increased slightly by 3 to 5 beats.

ing of the heart rate, it may not return after the heart rate has again increased to the level at which the block originally occurred. This may explain why, when the short precordial strips are compared, the presence or absence of left bundle-branch block does not seem to depend upon the heart rate. The processes which depress conductivity, *i.e.*, ischemia in angina, inflammatory edema in infarction, or an excessive dose of quinidine, vary quantitatively. Such factors, and probably others (*e.g.*, electrolytes), are undoubtedly involved.

In Patient A. D. the abolition of left bundle-branch block was spontaneous, with no compensatory pause beforehand. Conduction was normal for half an hour; then bundle-branch block recurred. If stimulation of the carotid sinus had been initiated coincidentally, the remission might have been erroneously attributed to this treatment. Intermittent left bundle-branch block, like syphilis, can manifest itself in various ways. There is no condition about which there are so many opinions to be challenged or refuted. Modern authors and investigators differ considerably on the subject. The various findings indicate that bundle-branch block may present different manifestations in the same subject at various times.

Intermittent bundle-branch block is a purely electrocardiographic diagnosis without any specific clinical manifestations. In a few instances, it is undoubtedly the result of coronary artery disease. In many instances, the etiology cannot be determined. It has been suggested that some of these cases may be the result of previous myocarditis, especially when due to diphtheria in childhood. Bundle-branch block may be confirmatory evidence of the presence of coronary artery disease, but this hypothesis rests purely on statistical grounds.

When the condition is intermittent, it has been said that the block occurs when the heart rate increases. This concept is favored by the fact that the portions of the tracing showing bundle-branch block are about 2 to 10 beats faster than when conduction is normal, and the rate is faster with normal conduction than with bundle-branch block (Fig. 2, lead I). It is questionable, however, whether this is truly a critical level, for in many instances conduction is normal when the rate is slightly elevated to the level present at the time of onset of the initial paroxysm of bundle-branch block.

SUMMARY

A case of spontaneous temporary remission of left bundle-branch block is reported, as confirmed by a normal QRS interval in the electrocardiogram.

The demonstration of the role of the critical heart rate in left bundle-branch block suggests that care be exercised in evaluating the role of therapeutic measures causing reversal of bundle-branch block. The extremely narrow range of the change in cardiac rate required to cause a change in conduction hardly permits the interpretation of improved circulatory dynamics.

When the left bundle branch is involved in a zone of ischemia, the conductivity of the bundle varies, and a slight change in rate can alter conduction in a diseased bundle. Therefore such changes are of no clinical significance.

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ATHEROSCLEROSIS: A COMPARATIVE STUDY OF CAUCASIAN AND JAPANESE CITIZENS IN THE HAWAIIAN ISLANDS—1959

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FOREWORD

A statistical study was made utilizing multiple sources of data on the same general population group of Caucasian and Japanese inhabitants of Hawaii. These groups were evaluated for relative incidence of atherosclerotic and hypertensive manifestations. By each approach it was demonstrated that the Caucasian exceeded the Japanese in atherosclerosis, whereas the opposite obtained with respect to hypertension.

Ischemic heart disease and hypertension constitute the two major disorders of medical practice. They frequently co-exist. Renal artery thrombosis may appear as a provocative agent in hypertension; when it is found it represents a pathogenetic relationship. Conversely, hypertension seems usually to predispose to accelerated atherosclerosis.

The present tripartate statistical study is an effort to shed additional light on this problem. The population for evaluation represented the two principal racial groups of Hawaii—the Japanese and the Caucasian. These two races have been used as a basis for prima facie evidence in previous reports.

Statistical studies have been criticized for the lack of uniform reporting, often representing current fashions in diagnosis (1). Poor correlation has been noted between the diagnosis on death certificates and the autopsy findings. The present study sought to obviate these objections by utilizing multiple sources of data on the same population group. The Board of Health in Hawaii has an excellent statistical department containing accurate records.

METHODS

I. The protocols of the last 2,000 consecutive autopsies performed on persons more than 20 years of age in Queen's Hospital, Honolulu, were reviewed. This represented an extension of an earlier series of 1,250 cases reported in 1954. The evaluation was similar to that used in the early study; that is, the degree of sclerosis in the coronary artery and the aorta was recorded as 0 to 4 plus. The author who recorded the grading did not know the race, sex, or age of the subject. The degrees of sclerosis were then correlated with the vital dimensions. The comparative findings in all the major races were reported in a paper presented before the annual meeting of the Hawaii Medical Association in April 1959 (2).

II. The Board of Health in Hawaii provided data concerning the causes of death (as obtained from death certificates) among an estimated total population of 293,717 Japanese and Caucasians over a five-year period (1952–1958). These were tabulated by race, sex, and age. In the various series averages were used for the five-year period, 1952 through 1957; the 1956 population figure was used as a basis for rates. The cases were defined as follows:

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The hypertensive series included all cases signed out as essential hypertension, hypertensive cardiovascular disease, cerebral thrombosis, or cerebral hemorrhage (stroke). The cardiac series included arteriosclerotic heart disease, myocardial infarction, coronary thrombosis and coronary occlusion.

III. A review was made of the discharge diagnoses for cases from two Honolulu hospitals—Queen's Hospital serving a mixed racial group, and Kuakini Hospital serving predominantly the Japanese segment of the population. The consecutive discharges in the years 1952–1958, involving 29,527 Japanese and 23,503 Caucasian patients, were evaluated (Table 3).

RESULTS

Table 1 represents the autopsy findings with respect to coronary sclerosis. At the bottom of the table are the data on persons showing little or no sclerosis contrasted clearly with the data on those showing severe sclerosis. Among the Caucasians there were significantly greater numbers with severe atherosclerosis than among the corresponding Japanese group.

Table 2 shows the higher death rate from "heart disease" among the Caucasians. The situation is reversed in "hypertensive disease," for which the Japanese have the higher death rate.

Table 3 shows the hospital discharge diagnoses. Unfortunately, a breakdown for age and sex was not available. Accordingly, the total numbers of discharges per racial group were used to compute the case rates. There was no reason to suspect that this would unduly bias the figures.

The heart disease rate for Japanese was 21 per 1,000 discharges; for Caucasians it was 40 per 1,000 discharges. The hypertensive disease rate for Japanese was 51 per 1,000 discharges; for Caucasians it was 35 per 1,000 discharges.

TABLE 1

Coronary Sclerosis in Caucasians and Japanese as Indicated by Postmortem Findings

	Caucasian				Japanese			
	Males		Females		Males		Females	
	No.	%	No.	%	No.	%	No.	%
Total number of cases	575	100	378	100	164	100	103	100
Degree of sclerosis								
Grade 0	22	4	37	10	17	10	24	23
Grade 1	58	10	55	15	38	23	23	22
Grade 2	119	21	80	21	53	32	21	20
Grade 3	135	23	62	16	31	19	14	14
Grade 4	237	41	142	27	24	15	20	20
Not recorded	4	0.7	2	0.5	1	0.6	1	1
Mild or nil (grades 0–1)	80	14	92	25	55	33	47	45
Severe (grades 3–4)	372	64	204	43	55	34	34	34

TABLE 2

Mortality Statistics for All Hawaii per 100,000 of Each Group per Year

Caucasian versus Japanese (five-year averages)

	Caucasian		Japanese	
	Male	Female	Male	Female
Population (estimated)				
Aged 20–45 yrs.	19,300	23,650	37,700	40,505
Over 45 yrs.	9,150	8,350	15,000	12,965
Deaths from heart disease				
20–45 yrs	41	9	17	4
Over 45 yrs.	1,267	735	701	409
Deaths from hypertensive disease				
20–45 yrs.	17	9	17	12
Over 45 yrs.	620	625	800	663

TABLE 3

Incidence of Hospital-Diagnosed Heart Disease and Hypertensive Disease by Race and Sex and Age-group

(From hospital discharge records on 29,527 Japanese and 23,503 Caucasians)

Race and Sex	No. of Diagnoses of Heart Disease		No. of Diagnoses of Hypertension	
	In patients under 50	In patients over 50	In patients under 50	In patients over 50
Japanese males	125	236	176	450
Japanese females	62	200	239	625
Caucasian males	84	495	80	339
Caucasian females	14	332	66	330

DISCUSSION

The data presented here demonstrate a definite predominance of ischemic heart disease in Caucasians as compared to their Japanese counterparts. The opposite is true with respect to hypertensive disease in the two racial groups. This is in accord with previous observations. In 1954 we reported a total of 4,565 hospitalized Caucasians, 75 of whom were admitted for coronary thrombosis; whereas, of 5,254 Oriental patients admitted concomitantly to the same hospital, only 19 had coronary thrombosis. In a 1954 clinical study conducted by members of the American College of Physicians on 10,000 consecutive medical office practice patients in Hawaii, a similar pattern was revealed (3).

The mortality rate from Japan for ischemic heart disease in males (age 55 to 59) is reported as 60 per 100,000, compared to the United States rate of 638 per

100,000 for a similar group. Cerebrovascular death rates for the same groups are 375 per 100,000 in Japan as contrasted with 123 in the United States (4). These figures serve to emphasize the different incidences of these disorders. They are certainly not a single entity, as has been proposed in the past.

Although the incidence of atherosclerosis is less among the Japanese, they are by no means exempt from the disease. Recently, an opportunity arose to compare the present findings with those of Dr. T. Imai of Kyushu University (5). His data show that there is no question that atherosclerosis occurs among the Japanese in Japan, though apparently, it is less severe. Other reports from Japan state that from 6 to 20 per cent of male arteries exhibit severe atherosclerosis. Imai found less severe coronary sclerosis than was present in the Japanese of the present autopsy study. He also found a greater disparity between atheromatosis of the aorta and that of the coronary vessels, whereas the autopsy figures in the present report demonstrate a close correlation (Table 4).

Recently, Keys *et al.* (6) found that the diet of the Japanese in Hawaii is in an intermediate position between the diet of the Japanese in Japan and those in Los Angeles. This also applied to their findings with regard to the amount of heart disease and the level of the serum cholesterol. The latter is correlated with the dietary fat, and a cause-and-effect relationship is suggested. Undoubtedly, the Japanese of Hawaii are now using the same diet as the Caucasians. The present study utilizes data derived largely from Japanese of the first and second generations. A similar study some years hence should reveal interesting changes, and possibly an equalization of disease rates.

There is some evidence that ischemic heart disease is increasing among the Japanese population of Hawaii.

Table 5 represents a seventeen-year study of the health records of sugar plantation workers in Hawaii, the fiftieth state. Half of the workers were Japanese, and half were Filipinos. The striking increase in both hypertensive and coronary disease is readily apparent. The increased age of the workers—a mean of nine years based on the data for eight plantations—could account for some of this rise. Improved diagnosis may also have been a factor. Improved economic conditions, with the associated dietary changes, likewise played a part. Sigler

TABLE 4

Degree of Aortic Sclerosis Compared with Degree of Coronary Sclerosis in the Postmortem Series, by Race and Sex

Race and Sex	Per Cent of Patients and Various Grades of Sclerosis				
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Caucasian males	3[4]*	9[10]	21[20]	22[23]	42[41]
Caucasian females	7[9]	11[14]	22[21]	21[16]	37[37]
Japanese males	6[10]	19[23]	31[32]	23[18]	18[14]
Japanese females	8[23]	27[22]	27[20]	20[3]	16[19]

* The percentages of patients showing coronary sclerosis are in brackets.

TABLE 5

Hawaii Sugar Plantation Association's Analysis of Incidence of Heart Disease (1942–1958) per 100,000 Population

(figures are averages per year)

Population (average)	Period	Type of Heart Disease (No. of Cases)				
		Bacterial endocard.	Coronary thromb.	Degen. myocard.	Hypertensive	Cerebrovasc. accid.
77,380	1942–46	5	26	88	586	82
68,535	1947–51	6	42	72	496	95
53,379	1952–56	6	82	86	1317	171
49,904	1957–58	7	132	96	2540	383
Increase during period from 1942 to 1958		40%	407%	9%	333%	367%

(7) found some correlation between the per capita income and the death rate from arteriosclerosis in the United States. The increase in hypertensive disorders is less easily explained. Adamson (8) has shown that serum cholesterol values in Japanese of the younger generation resemble those in Caucasians.

Ischemic heart disease is on the increase (9). This trend has also been observed in lower animals as reported by the Philadelphia Zoological Gardens (10). The cause of the increase is important. The present data show that although atherosclerosis is not so severe among the Japanese, nonetheless it exists. Stare (11) found that whereas the Guatemalan natives had fewer myocardial infarcts than a matched group of New Orleans workmen, until the age of 25 there was little difference in the amounts of atheromatous deposits. Though the United States population is distinguished by the predominance of advanced degrees of atherosclerosis, the total incidence of all lesions is not so different.

Widespread recommendations are now available as to the value of alterations of dietary patterns as a prophylactic measure against atherosclerosis (12–15). Even the confusing report of Page *et al.* to the American Heart Association contains an oblique reference to such a change (16). It is of interest that since this authoritative report was published, most of its authors have made more comprehensible individual recommendations (17). Dietary fat, particularly in the saturated fraction, should be reduced. There is some evidence that such a program is of real benefit in forestalling further complications in patients who have already suffered a myocardial infarct (18–20).

It is probable that the Japanese diet in Hawaii is changing, but as yet, no precise data are available. Whether the elevated blood cholesterol levels in the younger Japanese will be associated with higher death rates from vascular degeneration remains to be determined.

SUMMARY

The Japanese and Caucasian populations of Hawaii have been compared, utilizing several separate statistical sources. There is a higher incidence of

ischemic heart disease in the Caucasians, whereas there is a higher incidence of hypertensive disease in the Japanese.

These findings have been correlated with similar data from Japan and the United States. With respect to atherosclerosis, the intermediate position of the Japanese in Hawaii is confirmed.

The changing patterns of disease in these racial groups are discussed and etiologic factors considered.

Acknowledgments

The authors express their appreciation to Mr. Charles Bennett, Miss Lillian Louis and Mr. George Tokuyama in the Board of Health Statistical Department; to Dr. Harold Civen and Miss Ardes Alfrey of Queen's Hospital; and to Mr. B. R. Diehl of Kuakini Hospital.

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Abstracts of Current Literature

RICHERCHE ANATOMO-RADIOGRAFICHE SULL'ACCRESCIMENTO E SULLA SENESCENZA DELLE VENE DELLO STOMACO (ANATOMO-RADIOGRAPHIC INVESTIGATIONS ON THE DEVELOPMENT AND SENILE INVOLUTION OF THE VEINS OF THE STOMACH).

Azzali, G. *Arch. ital. Anat. Embriol.* **63:** 368, 1958; through Excerpta med. (Gerontol. & Geriatrics) **3:** 11, 1960.

Pursuant to studies concerning the senile involution of the arteries, an anatomo-radiographic study was made of the gerontologic characteristics of the venous vascularization of the stomach. It was found that the veins also undergo deformation: first the medium-sized ones, then the small ones, and finally the large ones become flexed and tortuous in progressive measure from maturity to advanced age, the alterations being very marked and generalized in advanced senility. In other words, old age does not spare the venous system, but here, also, destroys the distinct harmonious arrangements seen in the young, although the veins are affected later than the arteries. The presence was demonstrated of an anastomotic ring in the region of the lesser curvature, at the point of confluence of the right and left gastric veins, and also, in the pyloric region, of a vascularization made up of veins of smaller caliber (region of the small veins).

DEXAMETHASONE: ANTIRHEUMATIC PROPERTIES, HORMONAL EFFECTS AND ADVERSE REACTIONS (A SIXTEEN MONTH STUDY).

Black, R. L.; Reefe, W. E.; David, J. R.; Bloch, K. J.; Ehrlich, G. E., and Bunim, J. J. *Arth. & Rheum.* **3:** 112 (Apr.) 1960.

Dexamethasone was administered for eight to sixteen months in daily divided doses of 0.5 to 4.0 mg., with satisfactory antirheumatic response in 20 of 27 patients with rheumatoid arthritis. Five of the 27, although rendered more comfortable, failed to improve in functional status. This compound has been found to be the most potent anti-inflammatory corticosteroid thus far produced. It suppresses ACTH production by the anterior pituitary. Thyroid function, as measured by radioactive iodine uptake, was reduced in 11 of 19 patients. This suppression could be reversed by administration of TSH during continued steroid therapy. No direct evidence has been presented, however, to demonstrate that pituitary secretion of TSH is suppressed by dexamethasone. Dexamethasone caused impairment of carbohydrate metabolism in 11 of 22 cases, as reflected in abnormal glucose utilization rates on repeated determinations. In no patient, however, was elevation of the fasting blood glucose level or glucosuria observed. The most annoying side-effect in this group was striking weight gain—over 4 Kg. in 19 patients. The greatest gain was 18 Kg. Pathologic fractures occurred in 3 patients. In only 1 patient did a peptic ulcer develop during dexamethasone therapy. Psychosis did not occur. When dexamethasone was combined with salicylate therapy, it was possible to effect a substantial reduction of steroid dosage in 77 per cent of the patients so treated. On the other hand, occult blood in the stools was found in 8 of 11 patients receiving combined therapy, but in only 1 of 7 patients taking dexamethasone alone. One gastric ulcer was found among 22 patients who received periodic radiologic examinations. There were 2 deaths during the period of the study. Gradual withdrawal of dexamethasone was possible in 2 cases, after seven and twelve months respectively at a 2-mg. dosage level, without the appearance of adrenal insufficiency or recurrence of arthritis. Further observations are necessary to ascertain the effect of

long-term administration of dexamethasone on pituitary function and the incidence of serious side-effects. (From authors' summary.)

CLINICAL EVALUATION OF THE GASTROINTESTINAL TRACT IN THE AGED.
Cohen, T., and Gitman, L. *Am. J. Gastroenterol.* **33:** 422 (Apr.) 1960.

One hundred and two patients in good health and without evidence of recent gastro-intestinal disease were evaluated. Their ages were between 65 and 94 years, 82 being 75 years or older. The roentgenographic survey consisted of a gastro-intestinal series, barium enema, and gallbladder series. The findings were as follows: *Gastro-intestinal series*: Abnormalities were revealed in 58.7 per cent of the 92 examinations. There was no correlation with age or sex. The radiographic findings were (in numbers of patients): hiatus hernia, 15; peptic ulcer, 15 (14.7 per cent, a greater incidence than previously reported for the general population); gastritis, 10; duodenal diverticula, 5; widened duodenal loop, 3; prolapsed gastric mucosa, 3; displacement of the stomach by the liver, 2; small-bowel deficiency pattern, 1; esophageal diverticula, 1; and cardiospasm, 1. The esophageal hernias, the most common nonmalignant change observed, were asymptomatic and would have been missed without roentgenographic examination. *Barium enema*: Thirty-six per cent of the 75 examinations showed abnormalities. The 30.7 per cent incidence of diverticula of the colon is higher than previous estimates for all ages. The incidence increased with age. Diverticula frequently were seen in the exit of a blood vessel from the intestinal wall—a site which degenerative changes in the aged must have weakened. Diverticulitis was present in 7 patients, that is, in a percentage comparable to that found in the general population. Irritable bowel in 4 patients was not considered an unusual finding. *Gallbladder series*: Among 93 cholecystograms, abnormalities were seen in 38.7 per cent. Fourteen per cent showed stones, but the actual incidence probably was higher since patients with gallbladder disease were excluded, nonopaque calculi were present in gallbladders that did not become visualized, and some of the patients had undergone cholecystectomy in the past. The incidence of gallbladder disease was found to increase with age and to be higher in females (52.8 per cent) than in males (29.8 per cent). The incidence of stones was 22.2 per cent in females, and 8.8 per cent in males. *Composite of radiographic studies*: Forty-five per cent of the 260 studies showed abnormalities. All three examinations were completed in 64 patients, with abnormalities in 78.1 per cent; 9 per cent of the patients showed abnormalities in all three studies. No instances of the triad—colonic diverticula, gallstones and hiatus hernia—were encountered. *Symptomatology*: Clear-cut complaints usually were associated with pathologic states demonstrated radiographically. The incidence of vague complaints was no greater than in younger persons. Constipation was the most common complaint (43.1 per cent of patients) with an equal sex distribution. Altered taste perception was the complaint of 34.3 per cent; "bitter" was most frequently recorded. No significant decrement in gross taste perception was apparent with age. There was no relation between oral complaints and taste perception. The complaints were more common in the aged than in the younger group. Of the patients, 15.7 per cent complained of poor appetite, but some of this was admitted to be due to dislike of institution food. *Physical findings*: Hemorrhoids were present in 52.9 per cent of persons with a similar sex distribution. Constipation was found in 68.8 per cent of patients with hemorrhoids. Hernias in the abdominal wall were present in 17.6 per cent of patients, an incidence greater than that in the general adult population. The majority of these were in males and 72.2 per cent were of the inguinal variety. *Conclusions*: Except for constipation and altered taste, the complaints of older persons with reference to the gastro-intestinal tract are no more numerous than those of younger persons. The increase in abnormalities as a patient grows older is not striking; the prevalent findings are gallbladder disease, hiatus hernia, diverticula of the colon, inguinal hernia and external hemorrhoids.

MYOCARDIAL INFARCTION AFTER ACUTE GASTROINTESTINAL HAEMORRHAGE. REPORT OF 3 CASES.

Davison, K., and Smith, B. J. *Brit. M. J.* **1:** 1400 (May 7) 1960.

The clinical features and findings at necropsy in 3 cases of myocardial infarction occurring after acute gastro-intestinal hemorrhage are presented. Available evidence suggests that such posthemorrhagic cardiac disturbances are the result of inadequate coronary blood flow secondary to the reduced circulating blood volume, and that myocardial necrosis may occur if the changes are unduly great or prolonged. No coronary thrombosis was present but the myocardial infarcts were identical with those which follow coronary occlusion. Two of the patients had pre-existing angina of effort, and they were found to have marked coronary atheroma. Clinically 1 patient had no pain but 2 had prolonged retrosternal pain. Two patients had pulmonary edema, 1 congestive heart failure, 2 elevated temperature, and 1 subnormal temperature. All 3 had a polymorph leukocytosis. The electrocardiograms of 2 of the patients showed Q waves, one with S-T elevation. In the third, Q waves were absent and the changes were interpreted as due to left ventricular hypertrophy and ischemia without definite infarction. Early and adequate intravenous blood transfusion is indicated following acute hemorrhage in order to eliminate coronary insufficiency and prevent myocardial infarction. Transfusion also is recommended when myocardial infarction has occurred, because early restoration of coronary flow may restrict myocardial necrosis to a minimum. Since it increases coronary blood flow, the use of *l*-norepinephrine will help to protect the myocardium in the absence of a rapid response to transfusion. The pressor drug, metaraminol bitartrate (Aramine), has similar clinical action and experimentally has reversed the effects of induced coronary insufficiency.

CLINICAL EXPERIENCE WITH TRIETHYLENETHIOPHOSPHORAMIDE (THIO-TEPA) IN THE TREATMENT OF CANCER.

Edwards, M. H., and Rathmell, T. K. *Antibiotic Med.* **7:** (Apr.) 1960.

Twenty-nine patients with a mean age of 65 years and with advanced or inoperable carcinoma were treated with Thio-TEPA in total amounts ranging from 10 to 420 mg. given in a 10 per cent solution by intravenous or intracavitary injection, or injection directly into the tumor tissue. One patient subsequently was proved not to have a carcinoma but a penetrating peptic ulcer with chronic pancreatitis. Nine patients were benefited with a reduction in effusion or frequency of tappings, or both, decrease in size of the tumor, sensitization or resensitization to radiation therapy, relief of pain from bony metastases, and delimitation of the tumor permitting surgery. These carcinomas were neoplasia of the breast, ovary, tonsil, cervix, thyroid, pharynx, skin (malignant melanoma), and reticuloendothelial tissue (lymphosarcoma). One patient remains alive and well. The remainder died within five days to seventeen months; 20 survived less than six months. In 7 patients the dosage was deemed to have been inadequate (10 to 25 mg.). Two patients who received adequate amounts showed no effects. Nine patients showed evidence of tumor necrosis or bone marrow depression, but clinically they were not benefited or were even harmed by the agent. One patient lost to follow-up had had no recurrence for four months, but subsequently died in another institution. One case of fatal bone marrow depression occurred, the patient also showing visceral hemorrhages and ecchymoses. The drug was judged useful in the palliation of advanced carcinoma, but its use requires care.

POSTOPERATIVE CHANGES IN BLOOD COAGULATION IN ELDERLY PATIENTS.

Feruglio, G.; Sandberg, H., and Bellet, S. *Am. J. Cardiol.* **5:** 477 (Apr.) 1960.

Blood coagulability was studied in 15 patients aged 67 and 93 years, immediately before surgery and at three and seven days postoperatively. The coagulation studies were: clotting

time in glass and in siliconized tubes, recalcification time, prothrombin activity of the plasma (Quick), residual prothrombin activity, tolerance to heparin *in vitro*, and platelet count. The hematocrit values also were determined. In most patients, a state of hypocoagulability developed on the third postoperative day followed by a trend toward hypercoagulability on the seventh postoperative day. Not all of the clotting factors were oriented in the same direction on day 3; increased thromboplastin activity was manifested by shortening of the recalcification time. A drop in the platelet count and decrease in the tolerance to heparin appeared to counteract this effect and shift the clotting mechanism in the opposite direction. On the seventh postoperative day, all factors operated in the same direction, with shortening of the clotting time. This pattern occurred in 12 patients who underwent major surgery. Two who underwent minor surgery for the removal of cataracts showed no significant change in thromboplastin activity or platelet count. The trend toward hypercoagulability on the seventh day was greater in these old patients than in a similar study of younger persons. The tendency may account for a greater incidence of postoperative thrombo-embolic phenomena in elderly persons.

OBESITY AND DIABETES: A RE-EVALUATION.
Fineberg, S. K. *Ann. Int. Med.* **52:** 750 (Apr.) 1960.

Weight reduction is known frequently to ameliorate or reverse the diabetic state, with improvement in a patient's health. Stress is placed upon the correction of obesity in view of the growing use and increasing possibility of abuse of oral hypoglycemic agents. An agent with anorexigenic activity, which could serve as a substitute for the patient's incentive and for psychiatric treatment, was tried in a double-blind study for the control of obesity in diabetic patients. Twenty-nine patients received 25 mg. of phenmetrazine (Preludin) three times daily before meals for a mean duration of 9.7 weeks. Twenty-five control patients received placebo medication for a mean of 10.8 weeks. The two tablets were not identified prior to administration and the study had a third blind feature in that patients were given no hint of the purpose of medication. They received no diets nor dietary instructions. Those receiving insulin continued their daily dosages, which were approximately equivalent in patients in the two groups. Five additional patients in whom phenmetrazine therapy was started were dropped from the study because of side-effects, the most common of which were nausea and nervousness. No side-effects occurred in the remaining 29 patients, so that the incidence was 14.7 per cent in the entire group. The mean weight loss per patient in the drug-treated group was 7.4 pounds compared with 0.5 pound for the placebo group, or 0.78 pound compared with 0.07 pound per week. Twenty-five per cent of the 20 patients in the phenmetrazine group who received insulin were able to discontinue it, and an additional 25 per cent could reduce the dosage by 50 per cent or more. No control patient showed a significant reduction in insulin requirement. The results are interpreted to establish the value of an anorexigenic agent in the management of obese diabetic patients. Such an agent is deemed preferable to oral hypoglycemic substances in these instances.

PEPTIC ULCER AND HYPERPARATHYROIDISM. A SURVEY OF 300 ULCER PATIENTS.
Frame, B., and Haubrich, W. S. *A.M.A. Arch. Int. Med.* **105:** 536 (Apr.) 1960.

The diagnosis of ulcer was verified radiographically in all except 2 of the 300 patients. In screening them for hyperparathyroidism, the serum calcium and inorganic phosphorus concentrations were determined initially and the determinations were repeated if they were not in the normal range (greater than 11 mg. per 100 ml. or less than 3 mg. per 100 ml., respectively). Renal tubular reabsorption of phosphorus was determined for 125 consecutive patients in the series and for all who had abnormal serum calcium and phosphorus values, antacids having been withheld for twenty-four to seventy-two hours prior to the test. By these tests, 4 patients (1.3 per cent of the group) were found to have hyperparathyroidism, and a parathyroid adenoma was resected. In 2 of these patients, the evidence for peptic

ulcer was circumstantial; no ulcer could be demonstrated radiographically. This supports the view of Hellström (1959) that ulcer symptoms in the absence of an ulcer crater or deformity may be exhibited in hyperparathyroidism. This study leads to the conclusion that patients with peptic ulcer should be examined for the possibility of a co-existing endocrine disorder. In screening them, a careful system review is important, as well as the noting of unusual occurrences such as worsening of subjective distress by ulcer therapy rather than the usual prompt relief, or peptic ulcer disease that is unusually intractable to medical and surgical treatment or marked by the recurrence of ulcer at various sites in the gastro-intestinal tract which might arouse suspicion of a deleterious endocrine influence. The difficulties that will be encountered in evaluating calcium and phosphorus metabolism in patients receiving ulcer therapy are not insurmountable. Elevation of the serum calcium level has proved the most important biochemical clue to the diagnosis of hyperparathyroidism. The renal tubular reabsorption of phosphorus (TRP) test is nonspecific and too variable in results to use alone in diagnosis, but it can be used in conjunction with other biochemical determinations. No single determination is sufficient. When suspicion is high, repeated observations of biochemical data should be made before the diagnosis of hyperparathyroidism is supported.

THERAPY OF STOKES-ADAMS SYNDROME. REPORT OF FOUR UNUSUAL CASES WITH A REVIEW OF THE LITERATURE.

Goldberg, T. H., and Palman, R. S. *Am. J. Cardiol.* **5:** 540 (Apr.) 1960.

Current concepts in the therapy of Stokes-Adams syndrome are reviewed. Four cases illustrating some of the more difficult problems are presented. Recognition of the etiology of the A-V block and the mechanism of the syncope, whether it be ventricular asystole or acceleration, is important for successful management. Isoproterenol and epinephrine are the most valuable of the pharmacologic agents available and are used intravenously to control episodes due to asystole. Isoproterenol seems to have less tendency to produce ventricular fibrillation in human beings. Molar sodium lactate is useful in the patient who is no longer responsive to the sympathomimetic amines due to acidosis and hyperkaliemia. Adrenocortical steroids may have some value in heart block complicating acute myocardial infarction, on the basis of their anti-inflammatory action. Potassium deprivation can often improve A-V conduction. On this basis, chlorothiazide and adrenal steroids may be of value in chronic heart block. Quinidine and procaine amide are contraindicated in the presence of complete heart block. This may also apply to potassium. The external electric pacemaker is of great value in the management of episodes of syncope due to ventricular asystole but will have no effect on episodes due to ventricular acceleration. In the latter, the external electric defibrillator is effective. A small group of patients with Stokes-Adams disease and proved gallbladder disease may be helped by cholecystectomy. Resuscitation in the acute situation requires rapid action in a planned series of steps, while maintaining the airway at the same time. If asystole is suspected, pounding on the chest followed by cardiac needling, followed by an external pacemaker or open thoracotomy is the proper sequence. All this must be accomplished within four minutes. If ventricular fibrillation is the cause of the syncope, only external defibrillation or thoracotomy with cardiac massage will be effective unless the episode is very brief and spontaneous recovery occurs. (From authors' summary.)

THE CHANGES IN MORPHOLOGY OF THE THYROID GLAND WITH AGING.

Hee-Yong, P.; Kearns, J. E.; Teloh, H. A., and Davis, H. G. *Quart. Bull. Northwest. Univ. Med. School* **33:** 8, 1959; through Excerpta med. (Gerontol. & Geriatrics) **3:** 23, 1960.

Thyroid glands from 100 consecutive necropsies of patients of various ages, but mostly older than 40 years, were studied. In 75 per cent, nodules were found resulting from connective tissue proliferation, cyclic hyperplasia and involution of the gland. In 33 cases some

degree of lymphocytic infiltration was found, more often in females than in males. The severity of this infiltration was approximately parallel to the number of nodules present. The proportion of nodule-containing glands increased from 29 per cent for the 41–50 year old group to 76, 79, 88 and 87 per cent respectively in the following 10-year groups.

TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS WITH OESTROGENS AND ANDROGENS.

Hernberg, C. A. *Acta endocrinol.* **34:** 51, 1960.

Changes in height were the criterion for judging effects of estrogen-androgen combinations. Fifteen postmenopausal women with osteoporosis and 50 without, were treated for two to eight years. The initial dosage of estrogen was 0.25 mg. of estradiol benzoate, 0.005 mg. of ethinyl estradiol, or 0.001 Gm. of hexestrol per day. If no bleeding occurred, the dosages gradually were increased. Treatment was interrupted for two weeks after each six weeks of therapy. Thirty-nine of the 51 patients received in additional 3.5 mg. per day of methyltestosterone or 50 mg. of nor-androstenolone phenylpropionate in eight weeks. The 15 patients with osteoporosis were treated similarly but with higher doses of the hormones. Twenty-five postmenopausal women served as controls. The average height loss in the controls was 1.3 cm. six to eight years after the menopause, 5.2 cm. nine to twelve years thereafter, and 7.1 cm. fifteen to twenty years afterwards. Prophylactic administration of hormones for two to seven years to the women without osteoporosis prevented loss in height in all except one patient in whom a 1-cm. loss occurred. In patients with osteoporosis, hormone therapy caused cessation of height loss but usually not until the end of the second year of therapy. The effect was less distinct after two to six years of treatment in 4 patients. The use of androgen with estrogen facilitated the relief of back pain. Less masculinization occurred with nor-androstenolone than with methyltestosterone.

SEDATION AND ANALGESIA IN OLD AGE.

Howell, T. H. *Practitioner* **184:** 45 (Jan.) 1960.

Careful diagnosis must precede the prescription of sedatives to elderly people because of the many causes for restlessness. The indiscriminate use of hypnotics and tranquilizers is to be condemned because of the high incidence of mortality in these patients. Patients' preferences and fears with regard to certain drugs must be considered when prescribing, and the drug suited to the individual subject. Among sedatives and hypnotics, glutethimide (Doriden) in a dosage of 0.25 to 0.5 Gm. is one of the most useful. The routine administration of bromides for sedation is not advisable because of the likelihood of accumulation when renal function is impaired. Chloral hydrate serves for general use in insomnia and mild restlessness in a dosage of 30 grains, and chloral with phenazone for nocturnal discomfort. For wakefulness caused by pain, the dosage is 50 grains of chloral with 15 minims of tincture of opium. Barbiturates are best avoided as nocturnal sedatives. Short-acting drugs lead to addiction by day and are ineffective at night. Accumulation of the long-acting ones due to poor excretion leads to a reversal of the sleep rhythm. Paraldehyde is best reserved for extreme restlessness. In patients who show mental agitation, aggressiveness and motor over-activity, tranquilizers give the best results. Chlorpromazine and promazine, administered in minimal doses and with a careful watch for side-effects, are useful. Methylpentynol is indicated in case there is mental depression or apprehension. The multiple aches and pains of old age also require careful diagnosis. It must be realized that one of them may render another more troublesome, and that treatment of a specific one may render another more responsive. When general treatment with local measures, heat, local anesthesia and local applications fails, aspirin, phenacetin or phenazone (each in a dosage of 5 to 10 grains) are commonly prescribed. These have drawbacks in that they, respectively may depress the prothombin level of the blood with the risk of gastro-intestinal hemorrhage, cause methemoglobinemia and cyanosis, and cause agranulocytosis. Acetylsalicylic acid

compound tablets and codeine compound tablets may produce cyanosis because of their phenacetin content. The latter also have a tendency to cause constipation, which is undesirable in elderly persons. The addition of a small dose of an hypnotic is preferable to the use of a combination containing a hypnotic, because of the ability to control dosage. Phenylbutazone is a powerful analgesic, useful by intramuscular injection (1 Gm. in 5 ml.) in exacerbations of arthritis and in painful thrombophlebitis. Pethidine is particularly valuable in treating pain, because it leaves the mind clear and alert. It is used particularly in the terminal phases of inoperable carcinoma. Because of its short duration of action, it may have to be administered several times a day. Morphine, the ultimate analgesic, is valuable in calming the distress of cardiac failure, comforting the patient with nonproductive cough due to carcinoma of the bronchus, and providing relief in cases of inoperable carcinoma of the bowel. It is preferred to pethidine in terminal carcinoma. Its soporific effect may be enhanced by chlorpromazine, which also controls vomiting when present. Addiction is not a problem in the elderly, and normal doses may be employed in severe pain.

VESICOCOLIC FISTULA.

Hughes, E. S. R. *Dis. Colon & Rectum* **3:** 103 (March–April) 1960.

The causes of vesicocolic fistula in 11 patients were carcinoma of the bladder, 1; carcinoma of the sigmoid flexure, 2; carcinoma of the rectosigmoid area, 1; and diverticulitis of the sigmoid flexure, 7. The fistula was inflammatory in 7, partly inflammatory and partly malignant in 3, and malignant in 1. Two of the patients with carcinoma and 6 of the 7 with inflammatory fistulas were males. The patients with carcinoma were between the ages of 51 and 78 years. Those with diverticulitis were between 51 and 65 years. In general, the findings were of feces, air and blood in the urine and of urine passed through the rectum. Bowel symptoms were nearly always present. All except one patient had pain in the lower abdomen. The patients with diverticulitis typically had diarrhea. The patient with carcinoma of the bladder and vesicocolic fistula was incurable. Eight patients underwent a one-stage resection. Two patients had a colostomy prior to resection, one eight years and one four weeks previously. When malignancy was present, excision in the bladder wall extended well beyond the periphery of the involved area. In 3 of 6 cases with diverticulitis, the fistula was dissected free but the affected area in the bladder wall was not removed. Urethral and suprapubic drainage were used after closure of the bladder. Seven of the patients undergoing the one-stage operation recovered uneventfully, but 1 required a colostomy for a postoperative fecal fistula. Of the 3 patients with carcinoma of the bowel, 1 survived seven years, 1 six years, and 1 for nineteen months without recurrence. No malignant invasion of the bladder could be demonstrated. Five of 6 patients with diverticulitis recovered rapidly and have remained well for periods up to five and a half years. In the sixth patient, a series of complications developed, but recovery took place after colostomy for a fecal fistula. The patient who had had a transverse colostomy eight years previously and who had diminished renal function, did not survive the operation. In the patient with a colostomy four weeks prior to resection, the colostomy was later closed. The patient recovered, but two years later still had a sinus penetrating from the lower end of the wound.

HEMOCHROMATOSIS AND HEMOSIDEROSIS. STUDY OF 211 AUTOPSIED CASES.

MacDonald, R. A., and Mallory, G. K. *A.M.A Arch. Int. Med.* **105:** 686 (May) 1960.

A study of 211 cases of hemochromatosis and hemosiderosis occurring in 25,295 autopsies at the Boston City Hospital during the years 1917 to 1956 is presented. Cases were separated for analysis into three groups according to pathologic criteria: 57 cases of hemochromatosis (average age of patients, 60 years); 104 cases with a slight amount of hemosiderin in various organs, called simple hemosiderosis (average age of patients, 64.7 years); and an intermediate group of 50 cases with many, but not all of the features of hemochromatosis, called

advanced hemosiderosis (average age of patients, 61.3 years). Clinically active liver disease was not usually found in hemochromatosis. Approximately half of the patients entered with a presenting illness unrelated to liver disease. Most complaints on admission were due to neoplasm, infection and heart failure. The same was true of patients with advanced hemosiderosis and simple hemosiderosis. Eighty-five per cent of patients with hemochromatosis whose clinical records were available used alcohol to excess. Three-fourths of those who denied alcoholism had a history of a grossly inadequate diet or had a markedly fatty liver at the time of autopsy. Forty-three per cent of the patients who admitted alcoholism had stopped drinking for a number of years before admission. Among patients with advanced hemosiderosis 57 per cent, and among those with simple hemosiderosis 83 per cent admitted drinking alcohol in excess. Transfusions were not a significant factor in this study. In most patients excess iron in the tissues appeared to have been the result of absorption from the diet. The most frequent causes of death in the three groups were infectious disease and heart failure. The incidence of anatomic heart disease and of death from congestive failure was practically the same among the three groups. These was no evidence that patients with hemochromatosis had more heart disease or death from heart failure than patients of comparable age. The concept that hemochromatosis represents an inborn error of iron metabolism is questioned. It appears likely that hemochromatosis and hemosiderosis are variants of a single disease; in the "idiopathic" type of each there is abnormal absorption of iron from the diet. Findings in this study suggest that this may be caused by dietary rather than genetic factors. Hemochromatosis of the "idiopathic" type may be a variant of nutritional cirrhosis, in which the same dietary factors that contribute to the cirrhotic process lead to iron absorption. Other cases of hemochromatosis may be due to a combination of factors, such as anemia or hematologic disease causing excessive iron absorption, with transfusions or oral administration of iron further contributing to the amount of iron in the tissues. In addition there may co-exist factors that contribute to, or in themselves lead to cirrhosis. (From authors' summary and conclusions.)

L'ELETTROCARDIOGRAMMA NELL'ETÀ SENILE (THE ELECTROCARDIOGRAM OF OLD AGE).

Mezzasalma, G., and Morpurgo, M. *Gior. Gerontol.* Suppl. 14: 1–103, 1958; through Excerpta med. (Gerontol. & Geriatrics) **3:** 28, 1960.

The first part of this study is a comparative analysis of electrocardiograms in 400 subjects from 10 to 90 years of age with normal clinical and radiologic cardiovascular findings. The older the subject the greater the variability of the single ECG components. At an advanced age, the P wave shows increased bifidity and flattening particularly in L III, which may be a forerunner to fibrillation. The ventricular complex shows increased notching; this suggests an irregular intraventricular spread of the impulse. The duration of the P-Q and the Q-T period changes little, while voltage declines with age. Changes in the direction of the electrical axis are important; the P wave which at birth shows left axis deviation has a tendency to right axis deviation in old age, while the QRS axis moves in the opposite direction. These changes are not exclusively positional, due to change of body build, as shown by VCG; nor should the decline in voltage be solely explained on the ground of ischemic changes. Unknown factors related to physiologic involution may be at play. The second part of the study is devoted to pathologic changes in the aging heart. This is based on a statistical comparison between 4,401 unselected records of subjects aged 70 to 91 and the same number of those aged 20 to 40 years. Whereas 68 per cent of the latter group were normal, only 18 per cent of the former were so. Concerning the arrhythmias—with the exception of sinus bradycardia, all the other arrhythmias were much more frequent in the aged. The most common arrhythmias of old age were atrial fibrillation, extrasystoles, left bundle-branch block, partial A-V block, and right bundle-branch block in this order of frequency. The incidence of atrial fibrillation, of complete heart block, and incomplete left bundle-branch block increased gradually with age. Lone atrial fibrillation was often the only degenerative sign and was well borne. Left axis deviation, left ventricular hypertrophy

and left ventricular strain are much more frequent in the old than in the young, whereas the opposite applies to right ventricular patterns. The greater male preponderance in coronary insufficiency and cardiac infarction evens out at an old age, though the male preponderance, except during the last quinquennium, is still statistically significant. Anterior infarction was more frequent between the ages of 20 and 40, but after the age of 70 posterior infarction had a greater, though statistically not significant, incidence. Infarction without cardiac pain was relatively frequent in old age.

SOME OBSERVATIONS ON THE USE OF CHLORPROPAMIDE IN PRIMARY TOLBUTAMIDE-FAILURE DIABETICS.

Morgenstern, L. L. *Ann. Int. Med.* **52:** 761 (Apr.) 1960.

Among 12 diabetic patients in whom tolbutamide failed, chlorpropamide had effective hypoglycemic action in 6. The dosages used varied from 0.2 to 4 Gm. per day, but the higher dosages are not recommended for routine use. In 1 patient a better effect was obtained with chlorpromamide combined with insulin than with chlorpropamide alone. Two patients had a hypoglycemic response but clinical control was not satisfactory. Chlorpropamide was ineffective in 3 cases of brittle diabetes. Toxic effects consisted of the development of a papular rash in 1 patient. Chlorpropamide was discontinued in this patient because of an elevation of the serum glutamic pyruvate transaminase level; stabilization was achieved with insulin. The oral dosage of chlorpropamide bears no fixed relation to the blood levels. The minimum effective blood level is above 100 gamma per 100 ml. Values between 134 and 225 or 266 gamma per 100 ml. are required for satisfactory blood sugar levels. A substantial blood level persists for some time following cessation of therapy. The blood level is not, however, significant in determining the clinical response, and high levels do not guarantee a satisfactory response. The clinical response as measured by the blood sugar concentration is the best method for determining optimal dosage, which should be maintained at the minimum effective amount until more knowledge is gained of long-term effects. Clinical trial also is the best method of selecting patients likely to respond, although responsive patients appear to fall into the same general categories as those described for tolbutamide and carbutamide. Chlorpropamide is worthy of trial in brittle diabetes. These patients require extremely careful observation.

A QUANTITATIVE STUDY OF INITIAL AND TERMINAL QRS VECTORS IN A GROUP OF NORMAL OLDER MEN.

Mori, H.; Nakagawa, K.; Dahl, J. C.; Schmitt, O. H., and Simonson, E. *Am. Heart J.* **59:** 374 (March) 1960.

The initial and the terminal 10, 20, 30 and 40-msec. vectors of the QRS complex were statistically analyzed in 93 normal older men. These initial and terminal vectors were presented as mean values of azimuth, elevation and magnitude, with standard deviations for each angular and linear speed of the sweep. The initial QRS vectors point more forward, the terminal QRS vectors point more backward, and the magnitude of all instantaneous initial and terminal vectors is smaller in a group with wide QRS than in a group with narrow QRS. The electrical axis in the frontal plane did not correlate with the azimuth, magnitude or angular or linear speed of the initial or terminal vectors. The initial 40-msec. vector and the mean QRS vector are so similar in direction and magnitude that the 40-msec. vector cannot be truly considered as an initial vector. (From authors' summary.)

SYSTEMIC "RHEUMATOID DISEASE" WITH INTERSTITIAL PULMONARY FIBROSIS. A REPORT OF TWO CASES.

Ognibene, A. J. *A.M.A. Arch. Int. Med.* **105:** 762 (May) 1960.

One of these cases represents the first occurrence of diffuse interstitial pulmonary fibrosis to be reported in anarthritic rheumatoid disease. The diagnosis in each patient was confirmed by biopsy of the lung. Pulmonary function studies indicated a restrictive ventilatory

defect but the degree of impairment was different. The onset of pulmonary symptoms in Case 2 antedated the onset in Case 1 by three years. Arterial oxygen saturation and carbon dioxide content were normal in Patient 1, whereas in the second patient there was considerable unsaturation of the arterial blood with a high carbon dioxide content and resultant acidosis which persisted after clearing of congestive heart failure. Heart failure was not a feature of this clinical course until five years after the onset of dyspnea. Patient 2 also had advanced cor pulmonale. It was thought that the dissimilarity of cardiac involvement in these patients might be explained by a difference in the natural progression of the disease. The pulmonary symptoms in Case 1 occurred within two years after a normal roentgenogram had been obtained. It is thought that progressive pulmonary hypertension and ultimate right heart failure may develop in Patient 1 and become prominent features in the course of the disease.

SYMPTOMATIC TREATMENT IN THE MENOPAUSE.

Pollak, M. *Practitioner* **184:** 231 (Feb.) 1960.

The menopausal patient has two groups of symptoms: 1) those due to instability of the cardiovascular system, which seem to be due to a hormonal imbalance and can be controlled by estrogen, and 2) unaccountable fatigue and insomnia and an alteration in mood, causing irritability and depression. Because of the second group, meprobamate (400 mg. three times daily) was tested for the relief afforded in comparison with that from phenobarbitone (½ gr. three times daily) in 16 patients. In this double-blind study results were judged by noting changes in symptoms and the patients' general impression of well-being. For hot flushes, the two drugs were approximately equally effective. For insomnia, phenobarbitone was superior. All patients favored meprobamate for the relief of lethargy, irritability and nervousness, and for improvement in the sense of well-being. Drowsiness in 7 patients taking phenobarbitone necessitated discontinuation in 5 of them. One patient receiving meprobamate experienced drowsiness as the only side-effect. Thus, hot flushes are not affected by sedatives, although the patient may worry less about them. Barbiturates are are more effective for insomnia, but because of daytime drowsiness their administration should be limited to bedtime. Meprobamate is superior for the patient's well-being. The initial dosage of this drug should be 200 mg. twice daily in order to watch for untoward occurrences such as the development of a skin rash.

DISSECTING ANEURYSMS.

Rob, C., and Kenyon, J. R. *Brit. M. J.* **1:** 1384 (May 7) 1960.

Case reports are presented for 7 instances of dissecting aneurysm; 6 of the patients recovered following operation. Since medical management is ineffective, operation should be performed when the patient has a reasonable chance of recovery. End pressure in the blind lumen of the dissection must be relieved soon after it occurs in order to prevent rupture of the dissection into the pericardium with cardiac tamponade, or into the pleural or peritoneal cavities with fatal hemorrhage. Surgery, however, has no place in fulminating dissections, those with severe cardiac tamponade, and in patients whose condition has not become stabilized to some extent after the initial attack. It also is contraindicated when anuria has become established for more than a few hours. Aortography by retrograde arterial catheterization is the most certain method of confirming the diagnosis and determining the lower limit of the dissection. In the cases described, a re-entry ostium was formed in the lower limit of the dissection with obliteration of the distal dehiscence. The minimum area for such a re-entry ostium is 6 sq. cm. for the thoracic aorta and 4 sq. cm. for the abdominal aorta. To avoid the danger of rupture of the aorta or retrograde dissection with consequent hemopericardium on cross-clamping the aorta, a laterally placed nonocclusive clamp will sometimes be satisfactory. In 3 of the cases reported, this failed, and in 2 of them a temporary reduction in cardiac output was secured by removing blood from the aorta. It was transfused again after removal of the clamps. Twenty minutes of occlusion approaches the

upper limit of safety. In 2 cases clinical and aortographic examination following operation indicated that the aortic lumen had expanded to obliterate the dissection, with resultant broadening of the aorta. For this to occur, the outflow ostium must be larger than the inflow tear. Resection becomes necessary when aneurysmal dilatation of the false sac occurs. When the dissection involves the vessels of the lower limb, distal blood flow is best re-established with a prosthesis or homologous arterial transplant. The blind lumen of the dissection is decompressed in such cases.

ON THE INCIDENCE OF SENILE OSTEOPOROSIS.

Smith, R. W., Jr.; Eyler, W. R., and Mellinger, R. C. *Ann. Int. Med.* **52:** 773 (Apr.) 1960.

A survey was made of 218 ambulatory women over the age of 45 years. The roentgenographic evaluation was limited to a lateral view of the dorsolumbar spine centered at the thoracolumbar junction. The roentgenographic criteria used to rate the severity of vertebral osteoporosis were trabecular thinning, over-all loss of bone density, end-plate deformities, and major vertebral body deformities. The findings were as follows: normal density, 124-(57 per cent); indeterminate findings, 30; vertebral atrophy, 64 (29 per cent); vertebral wedging or compression fractures, 10 (4.6 per cent); and a progressive increase in incidence—7 per cent in the 45-49 year age group, 46 per cent in the 60-64 year old group, 28 per cent in women aged 65 to 69, and a maximum of 78 per cent in women over age 75. Among 123 women with symptomatic osteoporosis who received treatment, 23 per cent were under age 55 and in the greatest number the disease had been diagnosed between the ages of 60 and 65. A higher percentage of women with osteoporosis in the survey group were in the older age brackets. Only 3 women with normal vertebral density complained of back pain, although some indication of back pain could be elicited from 24 others—a total of 22 per cent of the nonosteoporotic women. This complaint was found among 34 per cent of women with demonstrable osteoporosis. Two of the 3 patients with Grade 3 osteoporosis were in the oldest age group; none of them gave a history of back pain. These figures, which represent an approximation of the incidence of osteoporosis for an ambulatory population in an institution, indicate that osteoporosis is a major disorder among the aging population as a whole. The accumulation of evidence that anabolic hormone therapy may arrest symptomatic osteoporosis makes clinically significant the observation of early vertebral atrophy in otherwise normal, asymptomatic women.

STEROID ARTHROPATHY OF THE HIP.

Sweetnam, D. R.; Mason, R. M., and Murray, R. O. *Brit. M. J.* **1:** 1392 (May 7) 1960.

The development of relatively painless destruction of the hip joint in 4 patients treated with corticosteroids is described. These changes differed from those that occur in rheumatoid arthritis and osteoarthritis in the absence of steroid treatment, in that they were more rapid, more extensive, and not accompanied by pain. The fact that pain occurred in 1 patient when steroid had been discontinued suggests that the relief of pain produced by steroids may be a significant factor in the destructive changes because of excessive activity in the absence of pain which might have led to excessive destruction (normally, this process would be held in check by reflex protective muscle spasm). In 2 patients the hips were normal before steroids were given. It is thought that the mechanism for the production of this arthropathy may be a combination of loss of joint pain, osteoporosis, and trabecular stress fractures acting together. It appears that a relatively high dose of corticosteroid over a prolonged time is necessary for the production of this change, although the time for disintegration varied from fifteen weeks to three and a half years. The time also is variable with intra-articular injection, one patient having received only three injections. Degeneration of the hip joint induced by steroids appears to be becoming more common. Therefore,

careful observation of patients receiving long-term or high-dosage steroid therapy is essential in order to detect early evidence of hip destruction and to adjust treatment accordingly. When considering the administration of corticosteroids, the possibility of this complication must be weighed against the possible benefit to be derived.

KLINISCHE BEOBACHTUNGEN ÜBER DIE ANGIOPATHIA DIABETICA (CLINICAL OBSERVATIONS ON DIABETIC ANGIOPATHY.

Szücs, S.; Csapó, G., and Tiszai, A. *Med. Welt* No. 9, 466–469, and No. 11, 573–576, 1960; through Ciba Literature Review **5:** 148, 1960.

An angiopathy can develop just as early in well-regulated and carefully supervised stable diabetic patients as in poorly treated or negligent patients. Retinopathy, however, can be prevented from progressing by means of proper check-up. The incidence of retinopathy is higher among female patients. The larger the number of pregnancies, the greater the tendency to diabetes. Diabetes itself is more common among women. These facts suggest that the endocrine system exerts a comprehensive influence on diabetes, but they do not explain why the angiopathy should occur at different times in different patients. The angiopathy depends apparently not on the mildness or severity of the metabolic disorder, but on the type of diabetes. Among their 176 patients, the authors found 82 cases of stable diabetes and retinopathy and 35 labile cases free of vascular disease. These figures agree with those of large-scale statistical studies. In both groups the disease had been present for less than ten years. These findings suggest that the two types of diabetes show a different pattern as regards vascular complications. In the authors' opinion, angiopathy is not a complication of stable diabetes but is a symptom, like hyperglycemia or glycosuria.

EFFECTIVE PLAN FOR CONTROL OF PRURITUS ANI.

Trimpi, H. D. *Dis. Colon & Rectum* **3:** 125 (March–April). 1960.

Fifty-six patients with severe pruritus ani (causes: nonspecific, 49; antibiotics, 3; moniliasis, 1; ulcerative colitis, 1; external hemorrhoids, 2) previously unresponsive to steroids, surgery, radiation and other methods of therapy, were treated with trimeprazine orally (average daily dose, 10 mg.) and triamcinolone acetonide locally three to four times daily. Eighteen patients drawn at random served as controls and received placebo medication rather than trimeprazine for one week. The duration of treatment ranged from three to fifteen weeks (average six weeks). Thirty-seven patients (66 per cent) obtained complete relief of itching, 10 (18 per cent) partial relief, and 9 (16 per cent) incomplete relief. There was no correlation between the results of treatment and the initial severity of pruritus nor its duration. Patients with partial relief obtained complete relief when the bedtime dose of trimeprazine was doubled. Twenty-eight of the 46 patients in whom pruritus was controlled with trimeprazine were able to discontinue steroid medication within three weeks, and 4 several weeks later. Four of 14 patients who required steroid therapy throughout the study period, were able to reduce the frequency of application. All control patients experienced a return of pruritus within forty-eight hours after trimeprazine was discontinued. The symptoms in 14 could be controlled in the daytime by increasing steroid medication. Trimeprazine was effective when therapy was reinstituted. There were no serious complications of trimeprazine therapy, which was given in tablets or sustained release capsules. This combination of therapy effectively broke the "itch-scratch" cycle. The control of pruritus ani was better than with steroid application alone. Most of the patients were able to continue working while under treatment. After this study was completed, 3 additional patients were treated. One resistant to local corticosteroids was controlled with 10 mg. of trimeprazine at night and 5 mg. in the morning. The other 2 were relieved with 10 mg. of trimeprazine at night and triamcinolone acetonide applied during the day.

EMERGENCY SURGERY IN THE ELDERLY.

Waterfall, M. *Practitioner* **184:** 199 (Feb.) 1960.

A survey of emergency operations in 115 patients shows that they are worthwhile, since the result is often success and the mortality rate is not prohibitive. These patients were aged 70 to 95 years. Five had two emergency operations. The six most frequent operations performed were for strangulated external hernia, large-bowel obstruction, appendicitis, cholecystitis, other small-bowel obstruction, and bleeding peptic ulcer. The conditions that carried the highest mortality rates were femoral embolus, bleeding or obstructing carcinoma of the stomach, bleeding peptic ulcer, perforated peptic ulcer, large-bowel obstruction, other small-bowel obstruction, and pancreatitis. The operative mortality was 22.5 per cent, but many of the deaths were inevitable because of the condition from which the patient suffered and others were caused by diseases not associated with the surgical emergency. The simplest operation that would relieve the condition was chosen. Operation was performed when the condition was such that the patient inevitably would have died because of it. Other important considerations were early diagnosis and treatment, minimal preparation time, extremely careful hydration when necessary (tending to less than optimal hydration rather than the risk of overhydration), careful preoperative transfusion when required (with packed cells when the circulatory volume would permit), intravenous digoxin for patients with uncontrolled fibrillation, coughing to clear the lungs when there was respiratory infection, clearing the lungs postoperatively with an endotracheal catheter or bronchoscope, and gentleness during the operative procedure. Blood electrolyte levels were watched carefully, saline avoided, potassium administered with caution when it was necessary, anticoagulants avoided, and oral feeding and ambulation undertaken as soon as possible after operation. Respiratory infection (pneumonia, bronchopneumonia, or purulent bronchitis) accounted for more deaths than any other factor. To combat it, inhalations were given, coughing encouraged, and patients turned frequently but otherwise kept lying flat in bed; propping against a back rest was avoided. Morphine and pethidine to control pain facilitated coughing and expectoration. Sputum retention was relieved by bronchoscopy when other methods failed. Antibiotics were not used routinely unless gross infection was present. Other frequent causes of death were pulmonary embolus, coronary thrombosis, fecal peritonitis, peritonitis, and carcinomatosis.

NEWS AND NOTICES

INTERNATIONAL RESEARCH CONFERENCE—*Muscle As A Tissue*

To be held at The Lankenau Hospital, City Line & Lancaster Avenues, Philadelphia, Pennsylvania, *Thursday and Friday, November 3 and 4, 1960.* Registration Limited to 400. No Registration Fee.

Thursday, November 3, 1960

9:00 a.m. STRUCTURE AND FUNCTION

Chairman: Clark E. Brown, M.D., The Lankenau Hospital.
Andrew F. Huxley, M.A., F.R.S., Cambridge University.
Emil Bozler, Ph.D., Ohio State University.
Robert W. Ramsey, Ph.D., Medical College of Virginia.

2:15 p.m. CONTRACTION

Chairman: Hugh E. Huxley, Medical Research Council, University College, London.
Andrew G. Szent-Györgyi, M.D., Institute for Muscle Research.
Robert E. Davies, Ph.D., and Dennis F. Cain, Ph.D., University of Pennsylvania.
Laszlo Lorand, Ph.D., Northwestern University.
Britton Chance, Ph.D., University of Pennsylvania.

8:00 p.m. DINNER

Presiding: Alfred Putnam, President, The Lankenau Hospital.
Speaker: A prominent Russian scientist has been invited.

Friday, November 4, 1960

9:00 a.m. PERFORMANCE

Chairman: David B. Dill, Ph.D., United States Army Chemical Center.
Erling Asmussen, Ph.D., University of Copenhagen.
E. Hohwü Christensen, Ph.D., Kungl. Gymnastiska Centralinstitutet, Stockholm.
Steven M. Horvath, Ph.D., The Lankenau Hospital.
Stewart G. Wolf, M.D., University of Oklahoma.

2:00 p.m. CLINICAL APPLICATION

Chairman: Philip S. Hench, M.D., The Mayo Clinic.
George E. Burch, M.D., Tulane University.
Ragnar Granit, M.D., Nobel Institute for Neurophysiology, Stockholm.
Stuart C. Cullen, M.D., University of California.
Kaare Rodahl, M.D., The Lankenau Hospital.

OPEN FORUM

8:00 p.m. PHYSICAL FITNESS IN HEALTH AND DISEASE

Chairman: Charles L. Wilbar, Jr., M.D., Secretary of Health, Commonwealth of Pennsylvania.
Moderator: Edward L. Bortz, M.D., The Lankenau Hospital.

Grant-in-Aid: The American Geriatrics Society.

BOOKS RECEIVED

Receipt of the following books for review is hereby acknowledged. We are glad to publish complete listings of all new books received but such listing must be regarded as a sufficient return for the courtesy of the sender. Books of particular interest will be reviewed in full as time and space permit. Additional information in regard to all listed books will be gladly furnished upon request.

STRIKE BACK AT ARTHRITIS. *U. S. Department of Health, Education, and Welfare. Public Health Service. In collaboration with: The Arthritis and Rheumatism Foundation.* Paper. 40 cents. Pp. 44. Illustrated. United States Government Printing Office, Washington, D. C., 1960.

SOCIAL AND MEDICAL PROBLEMS OF THE ELDERLY. By *Kenneth Hazell, M. R. C. P., M. R. C. P. E., D. P. M.*, Consultant Gerontologist to Wolverhampton and Walsall. Cloth. $4.20. Pp. 216. Illustrated. Hutchinson Medical Publications Ltd., 178–202 Great Portland Street, London, W. I., England, 1960.

BIOCHEMISTRY OF LIPIDS. Proceedings of the Fifth International Conference on the Biochemical Problems of Lipids held at the Fourth International Congress of Biochemistry, Vienna. Edited by *G. Popjak*. Cloth. $6.50. Pp. 228. Illustrated. Pergamon Press Inc., 122 East 55 Street, New York 22, New York, 1960.

HANDBOOK OF SOCIAL GERONTOLOGY. SOCIETAL ASPECTS OF AGING. Edited by *Clark Tibbitts*. Cloth. $10.00. Pp. 770. The University of Chicago Press, 5750 Ellis Avenue, Chicago 37, Illinois, 1960.

GERIATRIC NURSING. By *Kathleen Newton, R. N., M. A.* Formerly Associate Professor in Out-Patient Nursing, The Cornell University-New York Hospital School of Nursing, New York, N. Y.; formerly Department Head, Out-Patient Nursing Service, The Cornell University-New York Hospital Medical Center; formerly Staff Nurse, The Visiting Nurse Association of Plainfield and North Plainfield, N. J. Cloth. $6.50. Pp. 483. Illustrated. The C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, Missouri, 1960.

THE LIST METHOD OF PSYCHOTHERAPY. By *Elizabeth Sher, Theodora Hirschhorn, Annette Davis, Eleanor Messing, Enis Post, and Arthur Messing*, with an Introduction by *Jacob S. List*. Cloth. $7.50. Pp. 258. Philosophical Library, Inc., 15 East 40 Street, New York 16, New York.

SO . . . YOU'RE GOING TO THE HOSPITAL. By *Leonard Berlow, M. H. A.*, and *Vincent J. Bagli, M. D.* Paper. $1.00. Pp. 194. The Association of Military Surgeons of The United States, Washington, D. C., 1960.

POLYPEPTIDES WHICH AFFECT SMOOTH MUSCLES AND BLOOD VESSELS. Proceedings of a Symposium held in London. Edited by *M. Schachter, M.D., M. Sc.* Cloth. $8.50. Pp. 336. Pergamon Press Inc., 122 East 55 Street, New York 22, New York, 1960.

A DICTIONARY FOR MEDICAL SECRETARIES. By *Isabel Alice Stanton*. Cloth.

$6.50. Pp. 175. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois, 1960.

THE THYROID GLAND. British Medical Bulletin, May, 1960, (Vol. 16, No. 2). This issue is devoted entirely to The Thyroid Gland. Paper. $3.25. The British Council, 65 Davies Street, London, W. I., England, 1960.

Books for review should be sent to Edward Henderson, M.D., Editor-in-Chief, 236 Midland Avenue, Montclair, New Jersey.